**DOCTORAL THESIS**

# Infection and haemorrhagic complications associated with skin cancer surgery.

Dixon, Anthony

*Award date:*
2009

# Infection and haemorrhagic complications associated with skin cancer surgery

Anthony J. Dixon MB, BS, FACRRM, FACSCM
Skincanceronly
66 Roslyn, Rd, Belmont, 3216, Victoria, Australia

**A thesis by publication for the award of PhD at Bond University, Gold Coast, Australia.**

# Declaration of originality

I certify, as the author of this thesis, and as first author of the publications arising, that I was the person primarily involved in the study designs, implementation, analysis and manuscript preparation. I declare that the work presented in the thesis is to the best of my knowledge and belief, original (except as acknowledged in the text) and that the work has not been previously submitted for a degree or diploma at any institution.

Anthony J. Dixon

# Acknowledgments

I would like to thank the many people who have contributed substantially to the process of developing this program of studies on complications and outcomes from skin cancer surgery. These include my supervisors during the period of studies:

- Prof. Chris Del Mar MD Bond University
- Dr. Deborah Askew PhD University of Queensland
- Prof. David Wilkinson DSc University of Queensland

Working with me on the links between arc welding and skin cancer:

- Dr. Brian Dixon PhD Department of Defense, Sciences and Technology, ADF.

Nursing staff at Skincanceronly who maintained the database and arduous telephone follow up requirements of the prospective studies:

- Janine Thorpe BA, RN Nurse, Skincanceronly
- Samantha Casey RN Nurse, Skincanceronly
- Simone Crabbe RN Nurse, Skincanceronly

Special acknowledgement must be made of two people who contributed at all stages of the studies from early development in 2001 until completion in 2008.

**Prof. John B. Dixon PhD** Monash University.

My brother John was instrumental and supportive at all stages of the development, implementation and publication of the trials described in this thesis.

**Mary P. Dixon B Appl Sci (Nursing)** Skincanceronly

My wife Mary who supervised the maintenance of the research database, coordinated the nursing staff and ensured sound methodology and protocols were implemented throughout the process.

I would also like to thank my two daughters, Zoe and Emma. They have kept their patience with their father while he worked on these studies over the last seven years. In that time the girls have grown from toddlers to the point of approaching completion of primary school.

I was originally enrolled in PhD studies at the University of Queensland but transferred mid studies to Bond University. For this reason, the principal supervisor altered from Professor Wilkinson to Professor Del Mar. Doctor Deborah Askew and Professor John Dixon were advising and supervising these studies in both the University of Queensland and Bond University periods.

# Summary of research reported

Over four years from 2002 to 2006, a series of concomitant studies were undertaken to explore the complications and outcomes of skin cancer surgery. Specifically:

1. Through prospective studies, to identify risk factors for bleeding and infectious complications following skin surgery.
2. To determine through a randomized controlled trial whether mupirocin ointment versus paraffin ointment versus no ointment on a wound following skin closure affords the patient benefit.
3. To determine whether patients are at increased post operative bleeding risk should they remain on warfarin and / or aspirin prior to skin surgery.
4. To develop and then trial a novel approach (reducing opposed multilobed [ROM] flap) for below knee wound closures that may reduce the incidence of skin surgery complications on the leg and foot.
5. To investigate whether patients who suffer surgical complications are less likely to be satisfied with the service provision.

## Methods

A prospective database was maintained for every patient attending the referral based Skincanceronly centre from July 1st 2002. Details of past history and skin cancer risk factors were obtained. Medications such as aspirin and warfarin were recorded. Procedures were documented including outcomes and complications of procedures. The type and site of all procedures was noted. Over the first 18 months of the data collection, patients were offered enrolment in a randomized controlled trial of placing ointment on wounds prior to a dressing being applied. These patients were also surveyed 6 months following surgery regarding their perceptions of the outcomes of such surgery. A new technique for closing defects below the knee was developed. After the technique had been used for 20 months, we retrospectively reviewed data and outcomes of this technique compared with traditional approaches.

## Results

Skin surgery below the knee was found to be at increased risk of wound infection. Surgery on or near the ear was found to be at greater risk of post operative bleeding than other body sites. Warfarin therapy was found to be a risk factor for postoperative bleeding but aspirin did not alter bleeding incidence. Skin flap surgery and skin graft surgery resulted in both an increase in bleeding and infection incidence when compared to wounds closed directly. Placing mupirocin or paraffin ointment on a wound following suturing did not alter wound outcomes.

The reducing opposed multilobed (ROM) flap is a novel approach to close medium sized defects (11 to 45 mm diameter) below the knee. My data demonstrated a reduced flap necrosis incidence when compared to traditional closures. Overall complication incidence was also significantly reduced with this new technique.

Patients view of their scar outcome was a key indicator to their view of the overall skin cancer service provided. Patients rated wounds on the trunk poorly compared with wounds elsewhere on the body, including the face. Suffering complications did not alter patient perceptions of their skin cancer service.

## Discussion

Postoperative bleeding following skin surgery was uncommon and was usually able to be managed conservatively. Adapting to patient perceptions of their skin surgery requires more than responding to complaints. An explanation and information regarding trunk scars may assist patients understanding that wound outcomes can be less aesthetic in these regions.

Antibiotic wound infection prophylaxis could be considered for: all procedures below the knee, wedge excisions of lip and ear, all skin grafts, and lesions in the groin. In view of the risk of antibiotic resistance, mupirocin ointment is not indicated for clean surgical wounds.

There was no case for discontinuing aspirin before skin surgery, but the INR should be monitored in patients taking warfarin. Skin surgery on or near the ear faces increased bleeding risk.

Clinicians could consider the ROM flap for elective defects below the knee from 11 to 45 mm in diameter. Satisfaction with the scar had the greatest influence on a patient’s perceptions of their skin cancer service.

## Limitations

A single experienced clinician in a southern Australia locale might not reflect complications, outcomes and perceptions of other clinicians in different cultures, climates and circumstances.

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# Abstract


## *Background:*

Skin cancer surgery remains the commonest elective procedure undertaken by medical practitioners in Australia. The most important complication of skin cancer surgery is recurrence and this is extensively reported on.

However, there is little published about other complications including (a) infection, (b) bleeding and (c) poor wound outcomes though complications are said to be at greatest risk below the knee. Nor is there much information about patients' perceptions of their skin surgery complications.

## *Aim:*

This program of studies focused on three key areas of complications of skin cancer surgery; (a) infection, (b) bleeding and (c) surgery below the knee. Research methods included clinical trials with historical controls, observational studies and a randomized controlled trial

## *Setting:*

A single doctor private medical practice confined to managing skin cancers on referral from their general practitioners.

## *Studies undertaken:*

1) Wound infection

I first explored risk factors for wound infection following skin surgery. Through a three year prospective study I examined predictors of wound infection associated with managing 5091 skin lesions on 2424 patients. The overall incidence of wound infection was 1.5% (75/5091). Skin flap and skin graft surgery resulted in higher incidences of infection of 3% (47/1601) and 9% (6/69) respectively. Surgery below the knee proved the only body region of increased infection risk, at 7% (31/448). Post operative infection on the face was at low risk of 0.8% (18/2209).

2) Antibiotic ointment trial

To investigate whether this infection incidence could be reduced by application of ointment to the closed wound prior to dressing, I undertook a randomized controlled trial of mupirocin ointment (562 wounds on 262 patients) versus paraffin (729 on 269) versus no ointment (510 on 247). Neither ointment made a significant difference to any parameter tested, including infection incidence.

### 3) ROM Flap description

A novel skin flap repair (reducing opposed multilobed or ROM flap) was developed to attempt to address the increased incidence of wound infection below the knee. The flap was developed from first principles to minimise tissue tension and maximise tissue perfusion at the skin wound edge.

### 4) ROM Flap trial

The ROM flap was then subjected to a retrospective trial on 225 defects below the knee between 11 and 44 mm in diameter. The incidence of infection was not significantly lower in patients who had their defect repaired with the ROM flap at 9% (13/140) versus closure by traditional techniques at 13% (11/85) p=0.36. However, overall complication incidence at 14% (20/140) and end flap necrosis incidence at 1.4% were lower than in patients managed with this novel repair compared with traditional closures (32% and 7% respectively).

### 5) Warfarin and Aspirin

In a prospective trial involving 5950 skin lesions on 2394 patients over four years I maintained patients on their warfarin and aspirin medication prior to skin surgery unless the international normalized ratio was greater than 3.0. The overall bleeding incidence was 0.7% (40/5950). The following were independent risk factors for bleeding: age 67 years or older, odds ratio (OR) 4.7 (95% confidence interval, 1.8 to 12.2); *P*=0.002, warfarin therapy (OR 2.9, (1.4 to 6.3); *P*=0.006), and closure with a skin flap or graft (OR 2.7 (1.4 – 5.3); *P*=0.004). Aspirin therapy was not an independent risk factor for bleeding.

### 6) Bleeding locations

Next I investigated from this same data set of 5950 procedures whether certain body locations were at increased risk of postoperative bleeding. Only surgery in and around the ear demonstrated a significantly increased bleeding incidence at 2%, (OR 2.6 (1.2 to 5.7); *P*=0.012).

### 7) Perceptions

The final study addressed the patient's perceptions of their skin surgery through a prospective observational study. 778 consecutive patients were surveyed and 576 responded. Suffering infection, bleeding or other complications made no difference to the patient's perception of their skin cancer service. Scars on the trunk were more likely at 27% (21/77) to be rated neutral or negatively by the patient compared to non trunk scars at 7% (33/476) or on the face at 5% (15/305), p<0.001.

### *Limitations:*

A single experienced clinician in a temperate southern Australia locale might not reflect complications, outcomes and perceptions of other clinicians in different cultures, climates and circumstances.

### *Conclusions:*

Wound infection is at increased risk below the knee. Neither mupirocin nor paraffin ointment alter this risk or any other outcome assessed. The ROM flap reduces the incidence of overall complications for surgery below the knee but does not reduce the infection incidence.

There is no case for discontinuing aspirin before skin surgery but the INR should be monitored in patients taking warfarin. Skin surgery on or near the ear is predictive of bleeding. Suffering complications does not adversely impact on the patient's perception of their skin cancer surgery service.

## Publications making up this thesis.


1. Dixon AJ, Dixon MP, Askew DA, Wilkinson D. Prospective study of wound infections in dermatologic surgery in the absence of prophylactic antibiotics. **Dermatol Surg** 2006;32:819-27.
2. Dixon AJ, Dixon MP, Dixon JB. Randomized clinical trial of the effect of applying ointment to surgical wounds before occlusive dressing. **Br J Surg** 2006;93:937-43.
3. Dixon AJ, Dixon MP, Dixon JB. Prospective study of long-term patient perceptions of their skin cancer surgery. **J Am Acad Dermatol** 2007;57:445-53.
4. Dixon AJ, Dixon MP, Dixon JB. Bleeding complications in skin cancer surgery are associated with warfarin but not aspirin therapy. **Br J Surg** 2007;94:1356-60.
5. Dixon AJ, Dixon MP, Dixon JB. Skin surgery to the ear risks increased bleeding complications – a prospective study. **J Plast Reconstr Aesthet Surg** 2008:4
6. Dixon AJ, Dixon MP. Reducing opposed multilobed flap repair, a new technique for managing medium-sized low-leg defects following skin cancer surgery. **Dermatol Surg** 2004;30:1406-11.
7. Dixon A, Dixon JB, Dixon MP. Reducing Opposed Multilobed Flaps Results in Fewer Complications Than Traditional Repair Techniques When Closing Medium-Sized Defects on the Leg after Excision of Skin Tumor. **Dermatol Surg** 2006;32:935-42.

## *Research into clinical practice publications*


8. Dixon A. Let's get back to the basics in managing melanoma. **British Medical Journal** 2008:336:1033
9. Dixon A. One lump or two? A case study of infiltrating BCC on the nose. **Aust Fam Physician** 2006;35:505-6.
10. Dixon A. Dysplastic melanocytic naevus syndrome. **Aust Fam Physician** 2006;35:601-2.
11. Dixon A. Skin cancer in patients with multiple health problems. **Aust Fam Physician** 2006;35:717-8.
12. Dixon A. Managing skin cancer below the knee. **Aust Fam Physician** 2006;35:785-6.
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20. Dixon A. Check Program. **Aust Fam Physician** 2007;36:583; discussion 583-4.
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23. Dixon AJ, Hall RS. Managing skin cancer--23 golden rules. Aust Fam Physician 2005;34:669-71.
24. Dixon A. The Multicenter Lymphadenectomy Trial Spells a Halt to Sentinel Node Biopsy. **CML Dermatology** 2006;11:1-5.
25. Dixon AJ, Dixon BF. Ultraviolet radiation from welding and possible risk of skin and ocular malignancy. **Med J Aust** 2004;181:155-7.

# Background to this program of research

## *a) Overview:*

There is remarkably little known about skin surgery complications and their risk factors. I was driven to explore further the causes of skin surgery complications so as my patients and patients in general may benefit. By understanding more about complications we may be able to help minimise them in the future.

I am in private clinical practice in Geelong, Australia. Here I manage solely patients with skin cancers or suspected skin cancers referred from other health care professionals, - largely general practitioners. The setting provides for an opportunity to launch a program of clinical studies to address some unanswered questions regarding skin surgery complications. I manage a large numbers of patients with a very narrow range of presenting complaints and diagnoses. Variation in surgical experience and technique would not act as a confounder within this program as I was the only clinician managing the patients. I had the opportunity to closely supervise all staff involved in the research program face to face. This minimized scope for straying outside of methodology and protocols. The setting was ready made for a substantial program to investigate complications and outcomes following skin cancer surgery.

Medicare data indicate excision of skin lesions including skin cancers is the most common surgical procedure undertaken in Australia.[1] It was apparent that if further knowledge could be gained regarding skin surgery complications then there was a potential benefit for many Australians. These procedures are undertaken by a wide range of medical practitioners including plastic surgeons, dermatologists and general surgeons. General practitioners manage the majority of skin lesions and skin cancers in Australia.[1] The most common and least serious of these skin cancers are basal cell carcinomas (BCCs), followed by squamous cell carcinomas (SCCs) and the more serious malignant melanoma.[2, 3] Other uncommon skin cancers are also managed from time to time.[4-8]

Skin cancer can be managed with numerous surgical and non surgical approaches. These include wide local excision[9-11], frozen section micrographic controlled surgery (Mohs) [12-15], urgent paraffin micrographic margin controlled surgery[16, 17], topical imiquimod[18-23], topical 5 flurouracil[24, 25], photodynamic therapy[26, 27], cryotherapy[28-31] and curettage with or without ablation.[30, 32-35] My practice incorporated all of the above modalities with the exception of Mohs surgery and photodynamic therapy. These two are the least used modalities in clinical practice in Australia. As such, assessing complications from my surgery could reflect most skin cancer procedures in this country.

Surgical wounds are being closed directly [36], by random pattern skin flaps[37], axial skin flaps[38], myocutaneous skin flaps[39], full thickness or partial thickness skin grafts.[40, 41] This range of closures has been effected in my practice. Defects from 2 to > 200 mm in diameter were managed.

Measured outcomes from skin lesion excision include recurrence rates.[28, 33, 42-49] Few studies have focused on other (non recurrence) complications of skin cancer management.

Frequent yet poorly addressed questions that may affect outcomes included:

- When should antibiotics be prescribed?
- Should warfarin or aspirin be ceased for skin surgery?
- Are young females the people most likely to be unhappy with skin surgery scars?
- Does antibiotic ointment on a wound reduce the infection risk?
- Are there parts of the body that suffer more complications than others?
- Are there reconstruction techniques that result in fewer complications than others?

No definitive answers to these questions were available from the literature. The incidence of complications in skin surgery is reportedly in around 6% of procedures.[50, 51] Major life threatening complications are reportedly very rare.[52]

Bleeding complications have been described as the commonest complication of skin excision surgery, accounting for about half of all complications, (3%).[51] Infection incidence has been reported in the order of 2% of surgical excisions[51] but can be as high as 8.6% in Australia.[53]

The program of studies comprising this thesis was designed to answer these questions regarding complications of skin surgery especially bleeding and infectious complications. The core of this thesis is seven published original manuscripts.

I established a long term large prospective database powered to provide a suitable evidence base to examine risk factors for infection and bleeding complications following skin cancer surgery.
I also effected a randomized controlled trial of ointment on wounds to evaluate this common practice in dermatologic surgery.
Through a prospective trial I addressed whether or not remaining on warfarin and / or aspirin prior to skin surgery results in an increased post operative bleeding incidence.

Prior to establishing these clinical studies, my practice managed around 1,500 skin lesions per year, with just over half of these being malignant. I had managed around 5,000 skin cancers prior to establishing these clinical trials.

From the outset a long time course for these studies was envisaged. It would take many years to recruit sufficient patients to meet the power requirements of some of the planned studies. As such, I was aware that design, ethics approval, recruitment, analysis and publication would take up to seven years to complete regarding some of the studies.

The thesis also contains many educational pieces published with the aim of improving skin cancer knowledge for medical practitioners. The core published works are presented in this thesis in two columns and a different text colour and font to distinguish them from the single column non published text of this thesis.

My practice has been trading as “Skin Cancer Only”. Patients were and are not accepted for treatment without a referral from a health care professional, usually the patient’s general practitioner. It is a small private practice in Belmont, a suburb of Geelong, - the largest provincial city in Victoria. Coming from a rural background, I have a Fellowship of the Australian College of Rural and Remote Medicine (ACRRM). This College was only recognized for full specialist status in early 2007. I successfully completed the rural surgical program auspiced jointly by the Royal Australasian College of Surgeons and the Australian College of Rural and Remote Medicine in 1995.

## *b) Types of complications:*

Complications associated with skin surgery can be local or distant to the treatment site.

***Distant complications*** include metastatic disease[54-56], anaesthetic anaphylaxis[57] and death.[58] Anaphylaxis can follow administration of local[57] and general anaesthetic agents.[59] A significant adrenaline dosage in the local anaesthetic can result in raised pulse and pressure along with patient anxiety.[60] Large doses of lignocaine in the local anaesthetic can result in cardiac dysrythmias.[61]

***Local complications*** can be classified as infective, bleeding, pain related[62], wound complications, allergy[63-65], recurrence[47-49, 66-69] and others.

***Infections*** in skin surgery wounds range from purulent suture foci through local cellulitis and infective necrosis to regional lymphadenitis and septicemia[70, 71]. Unusually, infection might effect organs deep to skin such as osteomyelitis.[72]

***Bleeding*** complications include blood collection deep to the closed wound[73], (haematoma) and blood loss from the surface (haemorrhage). [51] Bleeding complications can be further classified as intraoperative, postoperative and delayed.[74] Blood loss is able to be estimated allowing for further classifications based on volume of loss.[75]

***Pain*** complications following skin surgery include severe and persistent pain.[76]

***Wound*** complications occur in both the wound healing phase[77] and long term complications.[78]

Wound healing complications include suture reaction[79, 80], flap necrosis[81], dehiscence[82], granuloma formation[83], persistent swelling[84], and ulceration[85], - all of which may be associated with delayed healing.[86]

Long term poor wound outcomes include suture markings[87], keloid[88], hypertrophy[89], wound depression[90], elevation[91], spread[79], hypo-pigmentation[92], discolouration[92], subcutaneous fibrosis[93], contour distortion and contracture[92], - all of which may result in a suboptimal aesthetic outcome.

***Allergic*** complications include allergy to skin preparations[94], latex or wound dressings[95, 96], pruritis[97] and contact dermatitis[98, 99]. Common symptoms of contact dermatitis are; itch rather than pain, skin vesicles adjacent to wound, weeping. Causes include dressings, skin preparations, topical applications applied and latex.[99]

***Recurrence*** (non distant) can be classified as local[69], locally invasive into adjacent structures[46] and in-transit.[48, 100, 101]

***Other*** complications include an array of uncommon outcomes that are often related to the specific surgical site. This includes ectropion formation[102] following surgery to the lower eyelid or cheek. Nerves may be damaged in skin surgery including the facial nerve[103], branches of the trigeminal nerve[104], the accessory nerve[105] and digital nerves.[106] Psychological consequences can also follow skin surgery.[107]

While all of these complications have been described in the literature, there is, in the main, limited data on the incidence of each following skin surgery and less data on the risk factors for such complications.

## *c) Methods*

The series of trials had a common and overlapping methodology prior to commencement.

The studies involved referred patients who attended the Skincanceronly clinic between July 1st 2002 and February 28th 2006.

Inclusion criteria were: patient aged 18 years or more, eligibility to give informed consent and ability to comply with treatment requirements; and the presence of a skin lesion for which procedural intervention was required.

- No patient was prescribed antibiotics prior to a procedure or following a procedure unless evidence of wound infection was apparent.
- No patient had his / her aspirin or warfarin ceased prior to or following surgery unless the International normalized Ratio (INR) was over 3.0
- Smokers were not asked to cease smoking prior to or following surgery.
- Details of past medical history were recorded including: diabetes, heart surgery, pacemaker, asthma, rheumatic fever, skin cancers, melanoma, and actinic keratoses.
- Medications being taken by patients were noted with specific questioning regarding warfarin, aspirin, immunosuppressants, and corticosteroids.
- Patients were asked if they smoked and if so how many per day.
- Patients were questioned regarding their hat wearing behavior and shirt wearing behavior.
- Patients were asked whether they had ever been sun burnt to the point of blistering.
- Patients were also asked whether they had worked in outdoor occupations and if so for how long.
- Patients were also asked regarding their sunscreen usage.
- Allergies to dressings and medications were also noted.

Data on patients including all the above information was recorded on a Microsoft Access database specifically designed from scratch on Microsoft Access by Dr. Anthony Dixon for the purposes of collecting and processing data for these series of studies.

One clinician (A.J.D) performed all procedures. Surgical techniques included punch biopsy, elliptical excision, incisional biopsy, full and partial thickness skin grafts, curettage and random pattern skin flaps. There were occasional axial or myocutaneous flaps undertaken as well as small number of partial thickness skin grafts. The site of all removed lesions was recorded and all specimens sent for histopathological examination. Where multiple tumours required excision, the most concerning lesion was excised first.[108, 109]

Some consideration was given to the standard method of skin closure that would be implemented throughout this series of prospective studies. Despite some skin surgeons routinely closing all skin defects in two layers and others routinely closing in one layer, there has never been a randomized controlled trial to compare outcomes of these two popular approaches. The best evidence available comes from randomized trials of one versus two layer closure in obstetrics[110], gynaecology[111] and vascular surgery[82]. The studies show very little if any difference. The largest of these studies and the study that most closely reflects skin lesion surgery is that by el Gamel[82]. In this well executed study, bilateral saphenous veins were harvested from 100 patients. Because intervention and control wounds were on the same patients, gender, age and other confounders were largely eliminated. There was no difference in wound complication rate.

Without a clear evidence base to determine whether wounds be routinely closed in one layer or two, an intermediate approach was implemented during these prospective studies. Most wounds were closed with a single layer of interrupted polyamide or nylon. Absorbable deep sutures were used in closure only if layers deep to the subcutis required direct closure. The absorbable sutures were either braided polyglycolic acid suture or monofilament poliglecaprone. Wounds selected for closure with two layers were larger wounds, those under greater tension and many on the trunk.

All patients were given a detailed postoperative instruction sheet regarding wound management, warning signs and details of return appointments. Patients were followed clinically until wound healing was completed, at least until removal of sutures and longer following skin flap or graft surgery, or if a complication developed.

The primary outcome measure of the studies was incidence of infection and postoperative bleeding. Other complications were also recorded.

Infection was recorded and classified as: purulent suture site, suture abscess, cellulitis, infective necrosis, large subcuticular abscess, regional lymphadenitis and septicaemia. When there was abscess formation or evidence of involvement beyond the local site, a wound swab was taken for culture; otherwise, the infection was assessed clinically. In the absence of suppuration, a wound was

considered infected if three out of the following signs were present: discharge, pain, erythema or induration. All wound infections were treated with oral dicloxacillin, 500mg orally four times daily, unless sensitivity or allergy deemed this to be inappropriate.

Any post operative haemorrhage or haematoma was recorded. A haematoma was regarded as small (up to 5 ml), medium (5 to 50 ml) or large (over 50 ml). A haemorrhage was regarded as small (up to 25 ml), medium (25 to 100 ml), or large (over 100ml).
Haemorrhage was further classified as delayed (1 to 24 hours after surgery) and late (more than 24 hours).

Other complications were recorded for each wound managed. Adverse scar outcomes were classified as: wound spread, suture markings, suture reaction, hypertrophy, keloid, discoloration, hypo pigmentation, wound depression, wound elevation, dog ears, and contracture.

Other local adverse outcomes recorded were post operative bleeding, allergy to dressing, allergy to skin preparation, contact dermatitis, local recurrence, subcutaneous fibrosis, granuloma, dehiscence, pruritus, persistent pain, nerve damage, ectropion, nodal involvement and distant metastases.

Post operative pain was also recorded as: no pain, minimal discomfort not requiring analgesia, mild pain relieved with paracetamol, moderate pain requiring stronger analgesia, severe pain unrelieved by analgesia, worst pain ever experienced.

### Questionnaire at 6-month follow-up

A questionnaire was sent to all patients managed in the first 18 months of the trials. This questionnaire was an integral part of the patient perceptions and ointment randomized controlled trial. The questionnaire was first designed following a focus group asking patients what outcomes from their skin surgery they felt should be addressed in a formal study of outcomes from the consumer perspective. The questionnaire was considerably altered by the ethics review process including the addition of the “added comments” section at the end of the form.

Six months after surgery each patient was posted a one-page survey to complete and return (Figure 1). Any patient not returning the survey was sent another at 8 - 9 months after operation. The survey asked patients to rate the pain experienced and any inconvenience of the dressing, to comment on

their experience, to assess the final aesthetic appearance of the first operated area as excellent, very good, good, fair, poor or very poor, and to rate the quality of the service.

A sub analysis of the first lesions excised was performed for patients who had multiple lesions during the study period. Patients who had undergone multiple procedures were asked to rate only the first procedure.

The core peer reviewed published research will be presented in this thesis in a different type and colour of font and in two columns and on shaded paper to distinguish this material from the remainder of this work which will appear in full page width on white paper with black type.

Figure 1 Survey of participants 6 to 9 months following lesion excision.

How would you rate the wound discomfort from the time of the surgery?

- No pain
- Minimal discomfort that did not require pain killers
- Mild pain, relieved by Panadol, Panamax or Herron Paracetamol
- Moderate pain that required stronger pain killers to gain relief
- Bad pain that could not be relieved with pain killers
- The worst pain I have ever experienced

How would you rate the inconvenience of the dressing from the time of the surgery?

- No inconvenience
- A nuisance, but did not interfere with things
- Very disruptive or embarrassing to me
- Could not tolerate the dressing

Rate our performance as either:
Excellent, Very Good, Good, Fair, Poor or Very Poor to the following 12 questions:

How would you rate the time taken from being referred to Skincanceronly Clinic until the time you were assessed by our Doctor?
How well was the procedure explained to you in advance?
How would you rate the time taken to have your skin surgery?
How effective was the local anaesthetic?
How would you rate the actual operation?
How would you rate the nursing / reception staff?
How well was the pathology result explained to you?
How good was the follow up care by Skincanceronly Clinic?
How good was the final look of the scar?
How would you rate the cost of your treatment at Skincanceronly Clinic?
How good was any written material provided?
Overall, how do you rate our service?

Please feel free to add any comments

## *d) Statistical analysis*

Demographic details were presented as percentage or mean ± standard deviation (SD) as appropriate. Chi-square method (Fisher exact) was used to test the significance of differences between proportions and categorical variables.

Analysis of the ointment random controlled trial (RCT) was conducted on an intention to treat basis. Patient characteristics and differences between groups in each trial were assessed with analysis of variance using Tukey post-hoc analysis, Kuskall-Wallis H test and chi-square test as appropriate.

Key outcome incidences were analyzed using the chi-square test. The antibiotic ointment (RCT) was compared with controls individually using 2 x 2 tables.

In addition this method was also used to assess univariate risk of bleeding / infection estimates and these were presented as odds ratios with 95% confidence intervals (bleeding).

Multivariate analysis (bleeding) was tested using binary logistic regression (forward and backward) and odds ratio beta-coefficients with 95% confidence intervals shown.

Receiver operator characteristic curves to assess an age cut off value that represented the best combination of sensitivity and specificity for risk of a bleeding complication.

The SPSS 12.0.01 and later 14.0.2 (Chicago, Illinois,) statistical software was used for all statistical analysis. A p-value of less than 0.05 was considered statistically significant in all studies.

# Chapter 1 Prospective study of wound infections in dermatologic surgery in the absence of prophylactic antibiotics.

## *Introduction: -*

In this chapter we look at the issues surrounding limited data on the risk factors for wound infection with dermatologic surgery. The limitations in existing data prompted a large prospective longitudinal study of skin cancer surgery infections.

There is debate regarding the role or otherwise of antibiotics prior to skin lesion excision. They have been advocated in clean-contaminated and contaminated wounds but not in clean wounds.[112, 113] In general, expeditious usage of antibiotics is recommended with most circumstances not justifying antibiotics.[114-117] Others suggest more liberal usage of antibiotics.[118] A reduction in infection incidence following both topical and systemic antibiotics prior to cutaneous surgery has been reported.[119] Prophylactic antibiotics are recognized as having a role prior to skin surgery in patients at risk of endocarditis[114, 120] and those who have had recent joint prosthetic surgery.[114] Others claim skin surgery is an insignificant risk of endocarditis and that heart patients do not need such prophylactic treatment.[117, 121] Recent joint prosthesis has also been refuted as an indication.[117] Physicians vary greatly in their usage of prophylactic antibiotics or otherwise and frequently ignore established guidelines.[113]

In order to improve our knowledge of the role or otherwise of antibiotic prophylaxis a better understanding of the risk factors for wound infection is needed. Once we have more accurate data on circumstances where a high infection incidence can be predicted, then we are better placed to develop more refined guidelines on antibiotic prophylactic usage.

Our prospective study of wound infections over three years was designed to evaluate possible risk factors. The trial was published in “Dermatologic Surgery” in June 2006[122] as follows:

# Prospective study of wound infections in dermatologic surgery in the absence of prophylactic antibiotics.

Authors:
Anthony J. Dixon[1], MBBS FACRRM
Mary P. Dixon[2], B Appl Sci (Nursing)
Deborah A. Askew[3], PhD
David Wilkinson[4] MBChB, FRACGP, MRCP, DSc, PhD

[1] Dermasurgeon, Senior Lecturer, School Of Medicine, University of Queensland
[2] Nurse Manager, Skincanceronly, Geelong, Australia
[3] Post Doctoral Research Fellow, School of Medicine, University of Queensland, Australia
[4] Professor of Primary Care and Deputy Head, School of Medicine, University of Queensland, Australia

**Abstract:**

Method

We undertook a 3 year prospective study of 5091 lesions, (predominantly non melanoma skin cancer) treated on 2424 patients from July 2002 to June 2005. No patient was given prophylactic antibiotics, and no patient ceased warfarin or aspirin.

Objective

The study aimed to identify wound sites / procedures where infection incidence was over 5%, such that these circumstances may warrant wound infection antibiotic prophylaxis.

Results

Overall infection incidence was 1.47%. Individual procedures had the following infection incidence: curettage 0.73% (3/412); skin flap repairs 2.94% (47/1601); simple excision and closure 0.54% (16/2974); skin grafts 8.70% (6/69); and wedge excision 8.57% (3/35).

Analysis of regions of the body demonstrated that surgery below the knee (n=448) had an infection incidence of 6.92% (31/448) ($p<.0001$). Sub-analysis demonstrated that all regions below the knee were at high infection risk. Elsewhere, groin excisional surgery had an infection incidence of 10% (1/10) ($p=.027$). No other body site demonstrated an infection incidence beyond 5% of statistical significance.

Procedures on the face demonstrated infection incidence of 0.81% (18/2209). Diabetic patients, those on warfarin and / or aspirin, and smokers showed no difference in infection incidence.

Conclusion

Based on a prediction of infection incidence over 5%, the following cutaneous oncologic procedures warrant consideration of oral antibiotic wound infection prophylaxis; all procedures below the knee, wedge excisions of lip and ear, all skin grafts, and lesions in the groin.

Other than under these circumstances, surgery to the nose, ear, fingers, lips, skin flap surgery, and surgery on diabetics, smokers, and those on anticoagulants have previously been considered for wound infection prophylaxis but do not warrant such intervention based on our data.

**Introduction:**

Low infection rates have been reported with the surgical excision of skin tumours, including Mohs' surgery[50, 71] with incidence ranging from below 1 to over 4% following skin surgery to clean wounds[115, 120, 123].

In a comprehensive review of the subject, Maragh[114]and colleagues points out there are two indications for antibiotic prophylaxis in skin surgery: (i) wound infection prevention (therapeutic) and (ii) distant site infection prophylaxis, predominantly endocarditis and recent joint prosthetic surgery considerations. Maragh and colleagues identifies oral dicloxacillin and cephalexin as suitable choices for wound infection prophylaxis in selected cases of dermatologic surgery. Antibiotic wound infection prophylaxis for dermatologic surgery can be topical (including within the wound itself[124]) and systemic. However, in a prospective randomized controlled trial, we have demonstrated a lack of efficacy of topical mupirocin in preventing wound infection in skin cancer surgery[125].

Usage of wound infection prophylaxis in dermatologic surgery varies greatly from surgeon to surgeon with some studies reporting widespread usage of antibiotics.[126] In general, antibiotics are not indicated for non-inflamed skin involving uncontaminated wounds.[115, 116, 127] Antibiotic prophylaxis has a greater role when the skin is inflamed or infected prior to surgery[114], the skin is contaminated[112], or if the patient is immunocompromised.[114]

The location on the body is a factor in considering antibiotics. Extremities are believed to be at higher risk of wound infection.[85] In particular the lower limb has been identified as at high risk of surgical wound infection.[84] Other body locations reported to be at higher risk of wound infection following dermatologic surgery include the following: nose[128], ear[71], lip[114], groin[129], and axilla.[130]

Aspects of the patients' health may also affect their propensity to wound infection. In particular, people with diabetes are considered to be at increased risk of wound infection. This has been demonstrated in diabetics who have lacerations[131], have cesarean sections[132], cardiothoracic surgery[133, 134], laryngectomy[135], and knee replacement surgery.[136] In contrast, diabetes was not shown to be a risk factor for wound infection in studies regarding bariatric surgery [137], leg vein harvesting [84], and lower extremity revascularization surgery [85]. The dermatologic surgery wound infection incidence in diabetics compared with non diabetics is not well understood, yet diabetes is recognized as a possible consideration when considering wound infection prophylaxis [114]. Smokers may also be at increased risk of wound infection such as has been identified in hip surgery [138, 139].

More data are needed to determine sites of the body and techniques of dermatologic surgery that place the patient at increased risk of wound infection. With this added information the clinician can make a more informed choice regarding situations whereby wound infection prophylaxis is appropriate.

Aim:

We aimed to identify circumstances where skin cancer surgery (SCS) wound infection incidence of over 5% is predictable, such that in those situations surgery might have oral preoperative antibiotic administration considered. Specifically, through a three year prospective analysis of wound infections in a referral based skin cancer surgery centre, we aimed to identify body locations, dermatologic procedures and patient circumstances that, in the absence of antibiotic prophylaxis, place the patient at greater than 5% risk of wound infection.

**Method:**

This prospective study of wound infections in SCS without antibiotic prophylaxis was approved as part of a larger trial by the Barwon Health District Ethics Committee.

This study involved patients, and their lesions, managed in the 3 years from 1 July 2002 to 30 June 2005 at the Skincanceronly Centre, Geelong, Australia. Patients were not administered antibiotics either before or following SCS. In the event that wound infection developed, antibiotics were prescribed as appropriate. If a lesion was clinically infected at presentation, antibiotics were administered. Surgery was not undertaken until the lesion no longer had clinical features of infection and antibiotic therapy had ceased.

Inclusion criteria:

All patients presenting during the study period were considered for enrolment.

Inclusion criteria required that the patient:

Be referred to the Skincanceronly Centre for management of skin lesion(s).

Have a skin lesion for which incisional or excisional surgery or curettage is deemed appropriate in the patient's management. Surgical procedures included: Mohs surgery; small and large excision and closure of lesions; curettage (with or without electrodessication); skin flaps; full thickness and partial- thickness skin grafts; and wedge excision surgery.

Exclusion criteria included:

Lesions managed entirely by cryotherapy.

Lesions treated with topical imiquimod or other non surgical means.

Lesions beyond 15 on any given patient were excluded to avoid over representation of some individuals.

Partial thickness and full thickness skin graft donor sites were excluded.

Patients requiring prophylactic antibiotics due to heart valve or recent prosthetic joint surgery.

One dermasurgeon (AD) performed all procedures in one of two operating rooms at either Skincanceronly Centre or Geelong Private Hospital. All surgery was undertaken using sterile surgical gloves, drapes and equipment. The dermasurgeon wore a surgically clean gown and a face mask. At Geelong Private Hospital the surgical gown was sterile and disposable hair cover was worn.

The site of all removed lesions was recorded and all specimens underwent histopathologic examination. All wounds were closed with nylon or polyamide

interrupted skin sutures. Absorbable deep sutures were used in closure only if layers deep to the subcutis required direct closure. The absorbable sutures were either braided polyglycolic acid suture or monofilament poliglecaprone. Following surgery, all wounds had an application of an occlusive dressing unless site specific or patient's allergy considerations made this impractical.

Because some patients had multiple tumors excised, the tumor deemed by the surgeon to be most urgent was removed first and a sub analysis of these lesions was carried out.

Patient details noted included warfarin and aspirin therapy, diabetes, and smoking status. In keeping with current practice[140], patients on medication affecting coagulation such as Warfarin or Aspirin did not have this medication ceased prior to surgery unless INR levels were excessive to therapeutic range.

Patients were followed up at least until removal of sutures. Patients were telephoned by nursing staff the day following surgery. Patients were strongly encouraged to return for removal of sutures. In the event that a patient attended elsewhere for removal of sutures, they were followed up by phone.

*Infection recording*

Any wound infection was recorded and classified in the following predetermined groupings: low grade infection with or without purulent suture site; suture abscess; large subcuticular abscess; infective necrosis; cellulitis; regional lymphadenitis; and septicemia. Wound infection was assessed clinically unless there was evidence of involvement beyond the local site. Under these circumstances, a wound swab for culture was taken. In the absence of suppuration, a wound was considered infected if three of the following features were present; discharge; pain; induration; and erythema. All wound infections were treated with oral dicloxacillin 500mg orally four times daily unless sensitivity, patient size or allergy deemed this to be inappropriate.

Infection incidence for each location / procedure undertaken was compared with all other locations / techniques using the chi square test. A site or method of SCS would be considered at high risk of wound infection if an existing incidence of 5% or more was reported.

**Results:**

Participants

A total of 5091 skin lesions from 2424 patients were treated by excision or curettage in the 3 year study period. The average age of patients was 57.5 years (median = 50 years) with 52.5% of patients being female. The 5091 lesions managed included 1263 squamous cell carcinoma(SCCs) (24.8%), 1194 basal cell carcinoma (BCCs) (23.5%), 132 melanoma (2.6%), 130 dysplastic melanocytic naevi (2.6%) and 2203 other benign lesions (43.3%). The benign lesions included 789 actinic keratoses, 110 cysts, 88 solar lentigenes, 63 angiomata, 26 lipomata, 31 warts and 280 benign non dysplastic pigmented naevi.

All patients were followed up at least until removal of sutures. Ten patients were not seen at or following removal of sutures and were followed up through telephone contact. All others were seen by surgeon and nursing staff in the follow-up period.

Two patients (three lesions) were excluded because antibiotic therapy was commenced prior to surgery. One patient had a heart valve prosthesis and another had been administered intravenous antibiotics by the anesthetist with the management of conscious sedation. One patient had more than 15 lesions and had all lesions after the 15$^{th}$ excluded from the study. No patient was excluded due to recent joint prosthetic surgery.

Infections

Out of the 5091 lesions, 75 wound infections were recorded (1.47%). There was no difference in the infection rate between men and women. Ten wounds were swabbed. One did not demonstrate a pathogen. The other nine demonstrated heavy growth of *staphylococcus aureus*. In eight of these cases, the bacteria were resistant to Penicillin but sensitive to dicloxacillin and cephalexin. At no stage were antibiotics adjusted based on culture results. Dicloxacillin was the antibiotic of choice other than for three Penicillin sensitive patients who were prescribed roxithromycin.

Two patients had serious infections. One patient had extensive cellulitis that did not respond to oral dicloxacillin. The infection later responded to oral ciprofloxacin. Cultures did not identify a pathogen. Another patient did not respond to oral dicloxacillin and was subsequently managed by another doctor. She required hospitalization, debridement and intravenous antibiotics. A partial thickness skin graft was applied. This failed to take and the defect on the shin healed by second intent over many months. These were the only two patients who did not respond to the initial empirical antibiotic selection.

Infection in relation to surgical technique and site on body:

Infection incidence from each surgical technique is summarized in Table 1, and at different sites on the body in Table 2. All sites below the knee demonstrated and increased infection incidence. In total, there were 31 infections below the knee, or 6.92% ($p<.0001$). The groin was the only other body location that demonstrated infection incidence over 5%.

We hypothesized that perhaps only the larger defects below the knee were experiencing a high infection incidence. A subanalysis revealed that 225 defects below the knee were over 11 mm in diameter. The incidence of infection in this subgroup was 11.6% with 26 wound infections identified. In contrast, 223 defects smaller than 11 mm in diameter below the knee demonstrated an infection incidence of 2.24% with five wound infections identified. ($p = .0001$).

The types of infection are detailed in Table 3. It was noteworthy that abscess formation was not a feature of all 31 infections below the knee in contrast to 22 of 44 infections above the knee ($p < .0001$). Low

grade infections below the knee either developed flap necrosis or cellulitis rather than proceeded to abscess formation.

While the infection incidence on fingers was 4.88%, this was not significantly different to elsewhere. Only 41 finger lesions were managed in the 3 year period. Similarly, tumors treated with Mohs surgery demonstrated no significant difference in infection incidence. All three infected curettage wounds were on the shin from 35 lesions curetted below the knee (8.57%). A sub analysis of procedures undertaken in the difficult region; nose, ear, lip, hand and below knee is detailed in Table 4. Excluding wedge resection and graft operations, there were five infections in 346 operations on the ear and lip (1.48%).

The types of skin flaps (n=1601) undertaken in this 3 year period were as follows; 445 transposition (27.8%), 295 O - S (18.4%), 282 bilobed (17.6%), 175 reducing opposed multilobed (ROM)[141] (10.9%), 93 twin advancement (5.8%), 92 V – Y (5.7%), 85 A – T (5.3%),and 134 others (8.4%).

"At risk" patients

Diabetes was reported by 135 patients (5.6%) who accounted for 285 lesions. There were three infections among these wounds (1.1%). This was not different from the non-diabetic population (p = 0.54). A total of 369 (15.2%) patients were on either warfarin (n = 64) or aspirin (n = 299) or both (n = 6). These patients had 799 operations and experienced 10 wound infections (1.25%), which did not differ from the general population of patients (p = .57). Patients taking warfarin had 162 operations with three wound infections (1.85%), those taking aspirin had 647 operations with seven wound infections (1.1%) and patients taking both aspirin and warfarin had 10 operations and no infections.

There was no difference in infection rates between smokers and non smokers (p = .24). A total of 296 (12.2%) patients declared themselves as smokers. These patients had 634 lesions managed, having six wound infections, (0.95%).

Other potential influencing factors

We recognized that as some patients had many procedures, they may be weighted excessively in the overall analysis. However, a sub analysis of the infection incidence of the first lesion on each patient treated was not different from the overall infection incidence demonstrated (not shown).

We also recognized that infection incidence may have been different between the two surgical venues studied. One hundred seventy-four tumors excised at Geelong Private Hospital resulted in five subsequent wound infections (2.9%) This was not dissimilar to the overall infection incidence identified, (p = 0.12).

**Discussion:**

This study aimed to identify circumstances where SCS wound infection rates of greater than 5% can be predicted and therefore, circumstances where prophylactic antibiotics may be indicated.

We identified all SCS procedures, including curettage, at any site below the knee had a high infection incidence. This was expected given the compromise in circulation that is recognized in these locations. Of note was the finding that when infection progressed below the knee, it developed into cellulitis or infective necrosis but not abscess. We postulate that this lack of abscesses is due to the tight skin below the knee and hence reduced dead space. The higher wound infection incidence below the knee is relevant, given the increased risk of wound dehiscence, delayed healing, flap necrosis and poor cosmesis that can occur in association with wound infection. These adverse outcomes can also result in a reduced confidence in the clinician and even legal action. Consequently, wound infection prophylaxis for below knee procedures should be considered.

Skin grafts and wedge excisions were the only types of procedures performed above the knee that were associated with a high infection incidence. This contributed to the higher rates of infection incidence on the lips and ears, compared with the rest of the body (with the exception of below knee procedures). Lip and ear closures that did not require a graft or wedge excision had the same infection incidence as elsewhere. It was noteworthy that diabetics did not suffer a higher incidence of wound infection than non diabetics, either above or below the knee.

Flap surgery has a significantly higher infection incidence than elliptical excision and closure. Invariably these are larger / more complicated procedures with skin tension and perfusion being considerations in explaining this finding. While skin flaps are designed to reduce skin wound tension (among other features), wound tension is still frequently higher than noted in small simple elliptical closures. The skin flap often “controls” wound tension across a large part of the repair in a large defect where tension would have been excessive centrally if closed by ellipse alone. An example of this controlling of wound tension is seen with the ROM flap below the knee previously reported by this author.[141]

This study has significant limitations. It involves a single dermasurgeon working in two surgical venues in one southern Australian regional city. This region has a temperate climate. The wound infection incidence reported may not reflect practice elsewhere, such as more tropical / humid climates. Wound infections were assessed clinically rather than by culture of wound swabs. A relatively short follow-up period on some cases may have led to an underreporting of late wound infections. The trial setting was that of a community based dermatologic surgery centre where wound swabs would not be routinely taken on wounds where infection is a concern. This mimics routine community dermasurgical practice in Australia. Other than warfarin and aspirin, other medications affecting coagulation such as non steroidal anti inflammatory medications were not recorded in this database.

Whenever the question of antibiotic prophylaxis is considered, disadvantages include the risk of antimicrobial resistance arising from such liberal

administration. Further, antibiotics subject the patient to adverse reactions including allergic skin manifestations. A significant improvement in wound outcomes would be needed in future studies to justify the extra intervention of prophylactic antibiotics, given these significant reservations. This study has identified sites and procedures of high risk; it does not determine whether antibiotic wound infection prophylaxis will afford the patient benefit in these circumstances. While there is existing evidence that antibiotic prophylaxis will reduce the subsequent wound infection incidence, a randomized controlled trial specific to these high infection scenarios is needed to determine whether the sites / procedures identified improve sufficiently with such prophylaxis.

**Conclusion:**

Our results suggest that a 5% or higher incidence of wound infection in the absence of antibiotic prophylaxis is more likely following;

all SCS procedures at any site below the knee, although small defects do not demonstrate the same infection rate as larger ones; wedge resections of lip or ear, all skin grafts; and lesions in the groin.

Therefore, oral antibiotics need to be considered prior to surgery in these circumstances.

While flap surgery has over five times the infection rate of elliptical excisions, the only locations where flap surgery suffers an infection rate above 5% are those below the knee. As such, wound infection prophylaxis for flap surgery above the knee is not indicated. Mohs' surgery requires special consideration. The repeated surgery and intermittent wound packing at a single site results in wounds being clean-contaminated and are as such, at an increased infection risk. Furthermore, wound infection prophylaxis may need to be repeated in these cases due to the duration from the commencement to the conclusion of surgery in some cases.[114]

Patients who are smokers, diabetics and those on aspirin or warfarin medication do not have an infection incidence different from the general population, and as such need not be considered for wound infection prophylaxis, other than under the circumstances for the population detailed above.

When deciding about antibiotic wound infection prophylaxis, the clinician needs to involve the patient in the decision making process. Advice to the patient should include the likelihood of infection and other factors such as whether or not the wound is contaminated, whether the patient is immune-compromised, whether the patient is considered at increased risk of endocarditis, and whether the patient has had recent joint prosthesis surgery. To assist clinicians to give the best possible advice to patients about the efficacy of antibiotic wound infection prophylaxis, more research that is specific to the sites and circumstances indicated is needed to provide a comprehensive evidence base to support decision making in this area.

TABLE 1

Infections by technique

| Technique | Total cases | Infection | Infection % | P value to rest |
|---|---|---|---|---|
| Curette | 412 | 3 | 0.73% | NS p = .19 |
| Skin flaps | 1601 | 47 | 2.94% | < .0001 |
| Ellipse | 2974 | 16 | 0.54% | < .0001 |
| Skin grafts | 69 | 6 | 8.70% | < .0001 |
| Wedge excision | 35 | 3 | 8.57% | = .0005 |
| All techniques | 5091 | 75 | 1.47% | |

TABLE 2

Infections by location

| Location | Total cases | Infection | Infection % | P value to rest |
|---|---|---|---|---|
| Below knee - TOTAL | 448 | 31 | 6.92% | < .0001 |
| Calf | 290 | 16 | 5.39% | < .0001 |
| Shin | 113 | 11 | 9.73% | < .0001 |
| Foot | 45 | 4 | 8.89% | < .0001 |
| Thigh | 96 | 2 | 2.08% | =N S |
| Groin | 10 | 1 | 10% | = .025 |
| Upper limb - TOTAL | 762 | 16 | 2.10% | = .12 |
| Fingers | 41 | 2 | 4.88% | = .07 |
| Hand | 328 | 8 | 2.44% | = .13 |
| Forearm | 215 | 4 | 1.86% | = .63 |
| Arm | 178 | 2 | 1.12% | N S |
| Head - TOTAL | 2502 | 19 | 0.76% | < .0001 |
| Scalp | 293 | 1 | 0.34% | N S (.1) |
| Forehead | 349 | 4 | 1.15% | N S |
| Temple | 105 | 2 | 1.90% | N S |
| Zygoma | 127 | 1 | 0.79% | N S |
| Nose | 479 | 1 | 0.21% | = .016 |
| Ear | 247 | 7 | 2.83% | = .025 |
| Lips | 165 | 3 | 1.82% | N S |
| Cheek, jaw, eyelids, elsewhere | 737 | 0 | 0% | = .0001 |
| Trunk / neck / elsewhere | 1273 | 6 | 0.47% | = .0006 |
| TOTAL | 5091 | 75 | 1.47% | |

TABLE 3

Details of infection at various sites

| | Low grade infection | Abscess | Infective flap necrosis | Cellulitis | Total |
|---|---|---|---|---|---|
| Below Knee | 14 | 0 | 1 | 16 | 31 |
| Thigh & groin | 0 | 1 | 0 | 2 | 3 |
| Upper limb | 4 | 5 | 1 | 5 | 15 |
| Trunk | 3 | 3 | 0 | 0 | 6 |
| Head & neck | 5 | 13* | 0 | 2 | 20 |
| Total | 26 | 22 | 2 | 25 | 75 |

* Only one abscess was large and subcuticular, an abscess at nasolabial border, incised and drained.

TABLE 4

Subanalysis of infections in difficult areas by procedure type. Number of infections in parentheses.

| | Nose | Ear | Lip | Hand & fingers | Below knee including percentage |
|---|---|---|---|---|---|
| Ellipse | 147 (0) | 88 (3) | 116 (0) | 166 (3) | 211 (5) 2.4% |
| Curette | 13 (0) | 3 (0) | 1 (0) | 14 (0) | 34 (3) 8.8% |
| Skin flap | 319 (1) | 102 (1) | 27 (1) | 171 (6) | 201 (21) 10.4% |
| Skin graft | 0 | 40 (2) | 0 | 18 (1) | 2 (2) 100% |
| Wedge excision | 0 | 14 (1) | 21 (2) | 0 | 0 |
| Total | 479 (1) | 247 (7) | 165 (3) | 369 (10) | 448 (31) 6.92% |

## *Summary*

My first published paper has identified circumstances in dermatologic surgery where antibiotic prophylaxis may be considered due to a predicted infection incidence of over 5%.

It would have been preferable if the analysis was undertaken on people as well as skin lesions. Given some patients had several lesions excised, there is not complete independence between the excision of one lesion on a given patient and further lesions on that same patient.

It would also have been preferable if the analysis undertaken in this study was multivariate rather than univariate.

This study does not in itself identify a significant advantage of antibiotic usage in such circumstances. A randomized controlled trial of antibiotics would be required to determine the extent to which, if any, infection incidence was reduced by preoperative antibiotics and hence whether or not routine usage should be recommended. Clinicians use both topical and systemic prophylactic antibiotics to attempt to reduce wound infections. There is limited evidence that one route is preferable.

I commenced to address, (and the next chapter details), this topical versus systemic question in my second study. Through a randomized controlled trial of antibiotic ointment versus control, we may be able to provide skin surgeons with advice regarding application of antibiotic ointment on wounds prior to a dressing being applied.

# Chapter 2 Randomized clinical trial of the effect of applying ointment to surgical wounds before occlusive dressing

In this chapter we pursue findings from the infection prospective study. We have identified circumstances where prophylactic antibiotics may be considered. Now we explore the value or otherwise of topical antibiotics on a closed wounds as an infection prophylaxis strategy.

To further evaluate the benefit, or otherwise, of the application of antibiotic ointment and petrolatum on wounds following suturing, we effected a prospective randomized controlled of the placing of mupirocin (antibiotic) ointment versus paraffin versus control (no ointment). This study was published in the British Journal of Surgery[125] in August 2006. The full text of this published manuscript follows:

# Randomized clinical trial of the effect of applying ointment to surgical wounds before occlusive dressing

**Abstract:**

Background: A blinded randomized clinical trial was undertaken to evaluate the effect of applying ointment to a wound before occlusive dressing in comparison with no ointment or sterile paraffin.

Methods: Some 778 patients with 1801 surgical wounds following excision of skin lesions were enrolled in the trial. No ointment was placed on 510 sutured wounds of 247 patients, paraffin ointment was put on 729 wounds (269 patients) and mupirocin ointment on 562 wounds (262 patients). Wound infection, scar, haemorrhage, dehiscence and other complications were assessed at suture removal. At 6-9 months after surgery, patients were surveyed to assess the wounds, with a response rate of 74%.

Results: There were no significant differences in outcome for all end points evaluated. The infection rate was 1.4 % with no ointment, 1.6 per cent for paraffin and 2.3 per cent for mupirocin ($P$ =0.490) Total complication rates were 3.5, 4.7 and 4.8 per cent for no ointment, paraffin and mupirocin respectively ($P$ =0.590). Some 10.9, 10.3 and 8.2 per cent of patients respectively had a neutral or negative perception of their wounds at 6-9 months after surgery ($P$ =0.650), There was no difference in postoperative pain, degree of inconvenience, overall level of satisfaction with treatment.

Conclusion**:** Putting ointment on a surgical wound before occlusive dressing does not benefit the patient. In view of the risk of antibiotic resistance, mupirocin ointment is not indicated for clean surgical wounds.

**Introduction:**

Ointment is often placed under an occlusive dressing after the excision and closure of a skin lesion [118, 142-144] in the belief that it improves the aesthetic outcome and that antibiotic ointment may reduce the incidence of wound infection. An infection rate of 2 - 5 per cent may be expected for uncontaminated wounds following skin lesion excision [71, 145] with higher rates below the knee and in the groin[85, 146]. A number of topical antimicrobial and antiseptic preparations are available, [147, 148] but there is little evidence to support their use on uncontaminated surgical wounds.

Mupirocin ointment is considered to be an effective and safe topical bactericidal antibiotic[149] that results in a reduced postoperative infection rate when used on contaminated lesions before excision.[144] It is as effective as oral antibiotics in the prevention and treatment of superficial skin infections[149, 150] and compares favorably with oral antibiotics for the management of post excisional and experimental skin infections[77, 151]. Although these favorable effects cannot be extrapolated to the prevention of infection in non-contaminated wounds, mupirocin is widely advocated for clean wounds to reduce infection rates.[118, 144]

Mupirocin resistance has been observed in methicillin-resistant Staphylococcus aureus (MRSA) isolates [152] ,and a high incidence of

mupirocin MRSA resistance has been reported in Malaysia[153]. Mupirocin has a role in interrupting the colonization of MRSA in affected patients, including preoperative surgical patients[154], but continuing widespread usage may reduce its effectiveness in this respect.[155 156]

Moist occlusive dressings are used routinely by the authors after excising skin lesions as they have been reported to improve healing and to result in fewer infections and other complications.[108, 156-161]

A blinded randomized controlled study was undertaken to determine whether the use of ointment, ointment containing an antibiotic (mupirocin), or no ointment under occlusive dressings would reduce the incidence of infection and other wound complications in patients with non-contaminated surgical wounds. Effects on patient comfort and long-term satisfaction with the appearance of the healed wound were also investigated.

**Methods:**

The trial was conducted in accordance with the Declaration of Helsinki and approved by Barwon Health Research & Ethics Committee. All patients gave signed informed consent.

From the authors' previous experience, an infection rate of approximately 4 per cent might be expected; a reduction to less than 1% would be clinically significant. It was determined that 500 surgical wounds in each of the three groups would provide an 80 per cent likelihood of detecting a four-fold difference in the incidence of infection between the antibiotic ointment group and the control group receiving no ointment or paraffin (alpha of 0.05). Recruitment therefore continued until at least 500 surgical wounds were represented in each treatment group. Individual wound repairs in the same patient were treated as independent events, whether performed synchronously or at a different time (up to 15 lesions per patient were permitted, to avoid overrepresentation of some individuals).

Newly referred patients who attended the Skincanceronly clinic between July 1st 2002 and December 31st 2003 (when sufficient numbers had been recruited) were invited to participate. Inclusion criteria were: patient aged 18 years or more, eligible to give informed consent and able to comply with treatment requirements; and presence of a skin lesion for which incisional or excisional surgery was deemed appropriate and that would result in a wound appropriately closed with interrupted polyamide sutures.

Patients were excluded if the skin was contaminated or infected before surgery, if the surgical site was not amenable to a moist occlusive dressing (eg. eyelid, lip), or if the patient had a known allergy to the occlusive dressing or one of the ointment preparations. Partial thickness skin graft donor sites were also excluded.

Patients (not wounds) were randomized prospectively to one of three groups before the placement of moist occlusive dressings: no ointment, sterile paraffin (Lacri-Lube®, *Allergon, Urvine, CA, USA*) and mupirocin ointment 20mg/gm (Bactroban®, *GlaxoSmithKline, Middlesex, UK*).

Allocation to a treatment group was undertaken by an independent person drawing one of 150 discs, (50 each of three different colours) from a barrel. Upon completing the barrel, the process was repeated. Neither surgeon nor patient was aware of randomization, although patients could

not be completely blinded to the application of an ointment by the nursing staff.

One surgeon (A.J.D) performed all procedures. Surgical techniques included punch biopsy, elliptical excision, incisional biopsy, full and partial thickness skin grafts, and random pattern skin flaps. The site of all removed lesions was recorded and all specimens sent for histopathological examination. Where multiple tumours required excision, the most concerning lesion was excised first.[108, 109]

All patients were given a detailed postoperative instruction sheet regarding wound management, warning signs and details of return appointments. Patients were followed clinically until wound healing was completed at least until removal of sutures and longer following skin flap or graft surgery, or if a complication developed.

The primary outcome measure was the incidence of wound infection, which was recorded and classified as: purulent suture site, suture abscess, cellulitis, infective necrosis, large subcuticular abscess, regional lymphadenitis and septicaemia. When there was abscess formation or evidence of involvement beyond the local site, a wound swab was taken for culture; otherwise, the infection was assessed clinically. In the absence of suppuration, a wound was considered infected if three out of the following signs were present: discharge, pain, erythema or induration. All wound infections were treated with oral dicloxacillin, 500mg orally four times daily, unless sensitivity or allergy deemed this to be inappropriate.

Other complications were recorded for each wound managed. Adverse scar outcomes were classified as: wound spread, suture markings, suture reaction, hypertrophy, keloid, discoloration, hypo pigmentation, wound depression, wound elevation, dog ears, and contracture.

Other local adverse outcomes recorded were post operative bleeding, allergy to dressing, allergy to skin preparation, contact dermatitis, local recurrence, subcutaneous fibrosis, granuloma, dehiscence, pruritus, persistent pain and nerve damage, ectropion, nodal involvement and distant metastases.

Post operative pain was also recorded as: no pain, minimal discomfort not requiring analgesia, mild pain relieved with paracetamol, moderate pain requiring stronger analgesia, severe pain unrelieved by analgesia, worst pain ever experienced.

Questionnaire at 6-month follow-up:

Six months after surgery each patient was posted a one-page survey to complete and return. Any patient not returning the survey was sent another, at 8 - 9 months after operation. The survey asked patients to rate the pain experienced and any inconvenience of the dressing, to comment on their experience, to assess the final aesthetic appearance of the first operated area as excellent, very good, good, fair, poor or very poor, and to rate the quality of the service. Each patient's categorical scores were converted to ordinal variables for analysis as follows: excellent, 10, very good, 8, good, 6, fair, 4, poor, 2 and very poor, 0.

Patients who had undergone multiple procedures were asked to rate only the first procedure. A sub analysis of the first lesions excised was performed for patients who had multiple lesions during the same operation. Further, the survey sent to patients pertained only to the first lesion excised.

Statistical Analysis:

Analysis was conducted on an intention to treat basis. Patient characteristics and differences between groups were assessed by means of analysis of variance using Tukey post-hoc analysis, Kuskall-Wallis H test and chi-square test as appropriate. All key outcome incidences were analyzed using the chi-square test and antibiotic ointment was compared with controls individually using 2 x 2 tables. All analysis was performed using SPSS version 12.0.1 (SPSS, Chicago, Illinois, USA.)

**Results:**

Some 778 patients were recruited from a total of 926 referred to the clinic over the study interval who required therapy that involved surgical repair of incisions; 148 patients were excluded (figure1).

Patient characteristics and numbers of incisions in each group are detailed in Table 1. One patient had more than 15 lesions treated and so only the first 15 were included within the study. There were no significant differences between the groups.

Each enrolled patient had a median of 1 (interquartile range of 1; range 1 – 15) surgical wounds managed over the 18-month study interval. Second and subsequent operations included surgery to different skin sites as well as some lesions (predominantly malignant melanoma) that were managed in two stages with two excisions and closure.

Some 69.4 per cent of wounds were closed with elliptical excisions and direct closure; 29.9 per cent of closures involved a random pattern skin flap, and 0.7% a skin graft. There was no difference between groups.

Post operative complications:

Complications per wound closed are detailed in Table 2. There was no difference in the number of total complications between groups (p= 0.590). Overall complication rates were 3.5 per cent in the no ointment group, 4.7 per cent for paraffin and 4.8 per cent for mupirocin. No patient experienced an allergic or other adverse reaction attributable to the ointment.

Infection:

There was a total of 32 wound infections, giving an overall rate of 1.8 per cent, with no significant differences between the groups (p=0.490) (Table 2). Infections were predominantly suture abscesses and cellulitis. All wound infections responded to oral antibiotics, predominantly dicloxacillin. No abscess required drainage, and no infection necessitated intravenous antibiotics or patient hospitalization. No patient had more than one infected wound.

A sub-analysis of the excision region found a significant increase in the risk of wound infection in lower limb lesions. The 225 leg lesions had an infection rate of 4.4 per cent, compared with 1.4 per cent for other body areas ($p<0.001$), although the group to which the patient was randomized did not influence the risk of infection in the leg. (Table 2).

A sub-analysis of the first lesion on each of the 778 patients revealed no difference in the incidence of skin infection, wound problems, bleeding or total complications between the three groups. The rate of skin infection of first wounds was 1.6 per cent for no ointment, 3.3 per cent for paraffin and 2.3 per cent for mupirocin (p=0.460). The mean incidence of infection for first wounds was 2.3 per cent, and there was no statistically significant difference from the pooled data (not

shown). Further sub-analysis of small excisions and skin flap closure also showed no differences between groups (data not shown).

Non-infective complications:

There were fewer scar complications in the no-ointment group than when ointment was used, a difference that appeared to be due largely to an increased risk of skin necrosis in the mupirocin group (p=0.007) (Table 2). Of the seven cases of skin necrosis, five were in flaps and two in elliptical excisions, (one scalp and one ear).

Survey at 6-months:

A total of 576 patients (74.0 per cent) returned the completed survey. Non responders were not significantly different to responders with regards age, sex, sites of wounds or complication rate (data not shown).

The application of ointment to the wound made no difference to the degree of wound pain or dressing discomfort experienced after excision (Table 3). Analgesics were used by 25.6, 29.7 and 25.3 of patients in the no-ointment, paraffin and mupirocin groups respectively (p=0.540). Few found their dressing disruptive, embarrassing or intolerable. (1.1, 2.5 and 2.6 per cent in the three groups respectively (p=0.540).

With regard to the appearance of the surgical scar at 6-9 months, there was no difference between patients in the three groups for any variable (Table 3). Patients who described their wound outcome as excellent, very good or good were grouped as positive wound responders. The incidence of neutral or negative scoring was 10.9, 10.3 and 8.2 per cent in the no-ointment, paraffin and mupirocin groups respectively (p=0.650), and 9.8 per cent overall.

**Discussion:**

To the authors' knowledge, no substantial evidence has been published regarding the value of applying ointment to clean surgical wounds after suturing. Current understanding of the role of antibiotic prophylaxis in skin cancer surgery has been reviewed by Maragh et al.[114], and there is little evidence regarding the use of topical antibiotics.

This study has shown that paraffin and mupirocin ointment provide no additional benefit to the patient. Existing advice regarding the role of ointments on wounds[142, 143], (largely antibiotic ointment) following skin lesion surgery and before dressing should be reviewed in the light of these findings.

This study has limitations. The primary analysis was on wounds not patients, even though it was patients who were randomized. One wound per patient could have been studied, but this would have involved so many patients that the decision was taken to treat each wound as a separate event. The sub-analysis of the first wound treated in each patient did give the same findings, and no patient with several incisions had more than one infected wound.

All operations were performed by a single surgeon in a rural city in southern Australia, a region with a temperate climate. The findings with topical antibiotic usage may not be applicable in tropical and subtropical climates[114]. The wounds in this study were not examined routinely by medical or nursing staff at 6-9 months after surgery, and long term outcomes were limited to the patient's perception at self - assessment. Ideally, both patient and professional long term wound assessments would have been undertaken. Wound infection was assessed clinically rather

than by the culture of wound swabs. The trial setting was that of a community dermatological surgery centre where wound swabs would not taken routinely where infection was a concern.

The incidence of wound infection was lower than expected when the study, including its power, was designed. With the identification of a placebo infection incidence lower than expected, the power to find benefit from ointment is reduced. However, the low incidence of infection in the no ointment group further raises the question as to why infection prophylaxis need be attempted in skin excision surgery.

Of concern was the finding that the rate of skin edge necrosis was higher in the mupirocin group. Although the incidence was only 1.1 per cent in this group, it included six of the seven cases of postoperative skin necrosis found in the study, raising the possibility that mupirocin may impede skin edge perfusion.

Individual patient considerations that influence the decision to use prophylactic antibiotics for skin surgery include risk of endocarditis, recent joint replacement surgery and wound contamination.

In keeping with other investigators,[86, 114] the present study found that surgical wounds on the leg had a significantly increased risk of infection. However, even these sites at greater risk of infection did not benefit from the application of an antibiotic ointment before wound closure.

**Conclusion:**

This prospective randomized controlled trial showed that a single application of paraffin or mupirocin ointment applied at the time of wound dressing made no difference to infection rates, pain experienced, wound discomfort, or long term wound aesthetic outcomes when compared with no ointment application. Mupirocin use was associated with a higher incidence of skin necrosis. These findings argue strongly against the use of ointment on a clean surgical wound before the application of a moist occlusive dressing. Considering issues of antibiotic resistance, topical mupirocin should no longer be applied to clean surgical wounds.

Figure 1: Participant flow chart

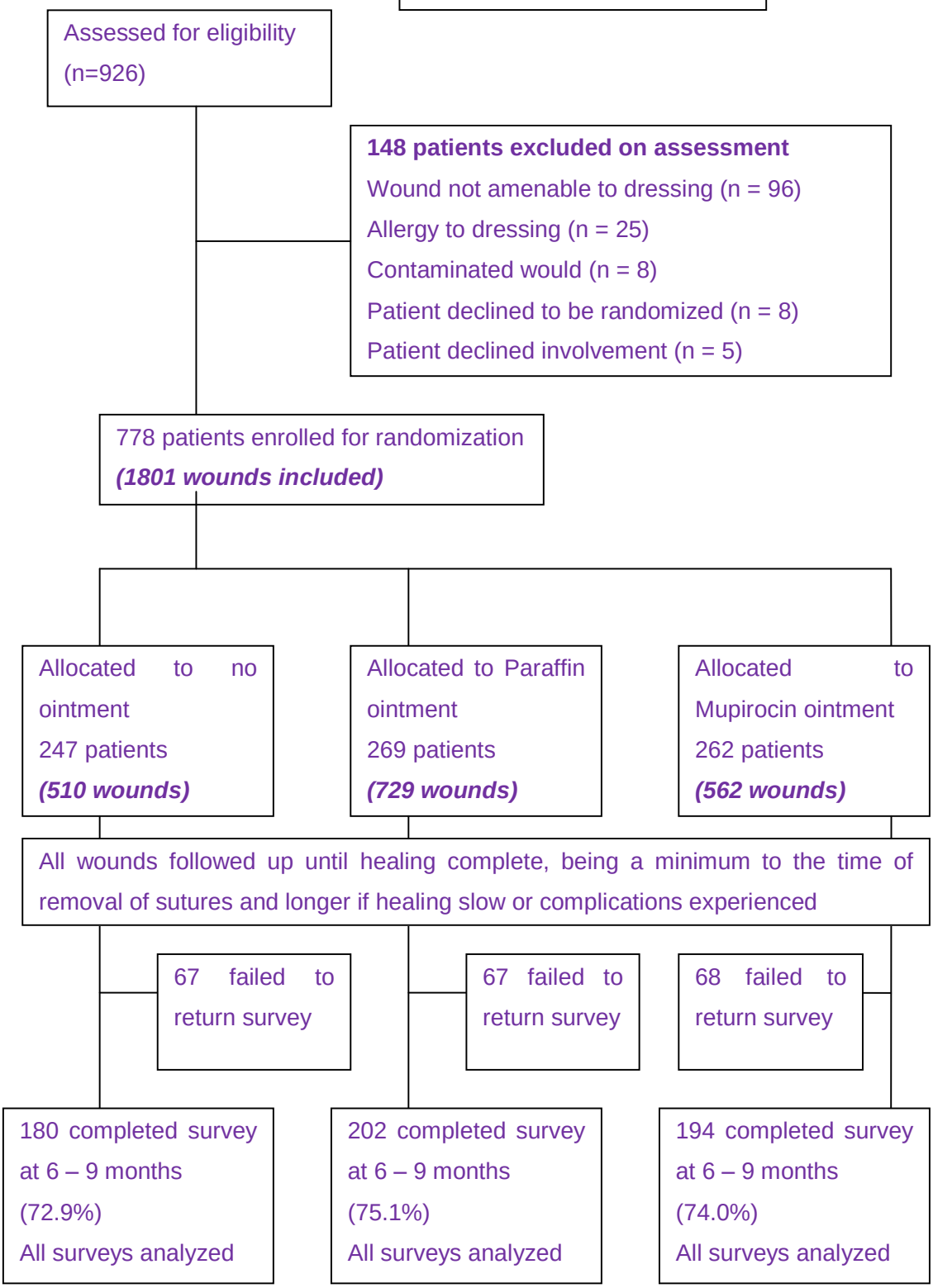

Table 1: Characteristics of and number of wounds per enrolled patients

| | No ointment | Paraffin | Mupirocin | Total | p-++ |
|---|---|---|---|---|---|
| No.of patients | 247 | 269 | 262 | 778 | |
| Mean (s.d.) Age (years) | 58.3 ± 17.3 | 60.5 ± 18.0 | 59.1 ± 18.3 | 59.3 ± 18.3 | 0.420 |
| No. of men* | 140 (56.7) | 138 (51.3) | 140 (53.4) | 418 (53.7) | 0.470 |
| No. of Wounds included in study | 510 | 729 | 562 | 1801 | 0.273 |
| Median no. of wounds per pt# | 1 (2) | 1 (3) | 1 (2) | 1 ( 1) | 0.110 |

Values in parentheses are * percentages and # interquartile range unless indicated otherwise.

Table 2: The incidence of post-operative complications per wound managed

| | No ointment (n=510) | Paraffin (n=729) | Mupirocin (n=562) | Total (n=1801) | P* |
|---|---|---|---|---|---|
| Wound infection | 7 (1.4) | 12 (1.6) | 13 (2.3) | 32 (1.8) | 0.490 |
| Suture abscess | 1 | 5 | 5 | 11 | |
| Cellulitis | 5 | 5 | 7 | 17 | |
| Infective necrosis | 0 | 2 | 0 | 2 | |
| Purulent sutured wound | 1 | 0 | 1 | 2 | |
| Lower limb (n=225)@ | 1 of 57 (1.8) | 5 of 102(4.9) | 4 of 66(6.1) | 10 of 225 (4.4) | 0.490 # |
| Scar complictns (other) | 0 (0) | 5 (0.7) | 7 (1.2) | 12 (0.7) | 0.044 |
| Skin necrosis | 0 | 1 | 6 # | 7 | |
| Hypertrophic scar | 0 | 2 | 1 | 3 | |
| Wound elevation | 0 | 1 | 0 | 1 | |
| Wound depression | 0 | 1 | 0 | 1 | |
| Post operative bleed | 6 (1.2) | 4 (0.5) | 2 (0.4) | 12 (0.7) | 0.230 |
| Wound dehiscence | 3 (0.6) | 6 (0.8) | 4 (0.7) | 13 (0.7) | 0.890 |
| Other complications | 2 (0.4) | 7 (1.0) | 1 (0.2) | 10 (0.6) | 0.510 |
| Total complications | 18 (3.5) | 34 (4.7) | 27 (4.8) | 79 (4.4) | 0.590 |

Values in parentheses are percentages. * Pearson's x2 test. # P=0.007 versus no ointment and paraffin. @ Excisions on the lower limbs.

Table 3: Patient reporting (for the first wound treated) of post-operative pain, dressing inconvenience and final appearance of surgical scar.

| | No ointment (n=180) | Paraffin (n=202) | Mupirocin (n=194) | Total (n=576) |
|---|---|---|---|---|
| Wound pain | | | | |
| No pain | 58 (32.3) | 63 (31.2) | 66 (34.0) | 187 (32.5) |
| Minimal – no analgesia required | 72 (40.0) | 76 (37.68) | 73 (37.6) | 221 (38.4) |
| Mild – paracetamol sufficient | 40 (22.2) | 53 (26.2) | 42 (31.6) | 135 (23.4) |
| Moderate – stronger analgesia required | 4 (2.2) | 5 (2.5) | 7 (3.6) | 16 (2.8) |
| Severe – not relieved by analgesia | 2 (1.1) | 2 (1.0) | 0 (0) | 4 (0.7) |
| Worst pain ever experienced | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Did not answer | 4 (2.2) | 3 (1.5) | 6 (3.1) | 13 (2.3) |
| Dressing problem * | | | | |
| No inconvenience from dressing | 99 (55.0) | 96 (47.5) | 87 (44.8) | 282 (49.0) |
| Nuisance – but no interference | 74 (41.1) | 94 (46.5) | 91 (46.9) | 259 (45.0) |
| Disruptive or embarrassing | 2 (1.1) | 2 (1.0) | 3 (1.5) | 7 (1.2) |
| Could not tolerate dressing | 0 (0) | 3 (1.5) | 2 (1.0) | 5 (0.9) |
| Did not answer | 5 (2.7) | 6 (3.0) | 10 (5.2) | 21 (3.6) |
| Appearance of surgical scar at 6-9 months | | | | |
| Excellent or very good | 130 (72.2) | 151 (74.85) | 146 (75.3) | 427 (74.1) |
| Good | 25 (13.9) | 24 (11.92) | 23 (11.9) | 72 (12.5) |
| Fair | 10 (5.6) | 16 (7.9) | 14 (7.2) | 40 (6.9) |
| Poor / very poor | 9 (5.0) | 4 (2.0) | 1 (0.5) | 14 (2.4) |
| Did not answer | 6 (3.3) | 7 (3.5) | 10 (5.2) | 23 (4.0) |
| | | | | |

Values in parentheses are percentages. There were no significant differences between the groups. * One patient from the paraffin group and one from the mupirocin group commented on the dressing, but did not select a category.

## *Summary*

In chapters 1 and 2 we have identified circumstances where an increased risk of wound infection might be expected. We have also indicated that topical antibiotic ointment on a closed wound does not appear to be a useful antibiotic prophylaxis strategy.

There is an issue in this study in that at times patients had several lesions excised. Repeated lesion excisions on the same patient results in a lack of absolute independence. This problem has been partly addressed in this study by the further analysis of the first lesion on each patient. However, the study was not powered to see significant results on a patient level.

The question remains regarding the role or otherwise of prophylactic systemic antibiotics prior to skin surgery. Administration of such antibiotics may be parentral or oral. For simple excisions only an oral administration is likely to be acceptable to patients. A randomized controlled trial of this administration route would be beneficial in the future to address some outstanding questions.

In my prospective study of infections[122], we identified that wounds below the knee are at the highest risk of infection following excision of lesion. Findings are consistent with the more recent study by Heal et al.[53]

Is there a way to reduce the infection incidence below the knee? Could a variation in technique improve outcomes? These are some the questions that arose following the first two published studies.

The following chapter details the design and theory behind my novel theoretical complication minimizing below knee closure.

# Chapter 3 Reducing Opposed Multilobed flap repair, - a new technique for managing medium sized low leg defects following skin cancer surgery

The previous studies raise concerns regarding surgery below the knee. An increased infection incidence was noted. This chapter explores a novel skin closure approach for defects below the knee. We postulate that the technique may reduce surgical complications in this region, including the high infection risk identified in chapter 1.

Traditionally medium and larger skin defects below the knee have been closed with split skin grafts. However, it is reported that skin flap repairs have advantages over graft closures in these locations.[11]

It is recognized that a flap with a substantial length relative to its base has an increased risk of end flap necrosis.[162] A flap design below the knee needed a minimal length:base ratio. This was the overwhelming principle used when we were designing a flap for usage below the knee. The flap was designed from first principles from years 2000 to 2002. Once a basic lay out was considered, it was subjected to further computer modeling and then spring tension analysis.

The design eventually developed was called the reducing opposed multilobed flap repair or ROM repair. The flap technique and the principles that resulted in the design were published in “Dermatologic Surgery” in November 2004.[141] The manuscript is as follows:

# Reducing opposed multilobed flap repair, - a new technique for managing medium sized low leg defects following skin cancer surgery.

**Abstract:**

Following skin cancer excision, skin defects on the low leg between 10 and 35 mm in diameter can be problematic. Direct closure of the wound risks excessive wound tension and wound dehiscence. Skin grafts heal slowly and often remain unsightly. Traditional skin flaps have a limited role.

The Objective was to develop a random pattern skin flap that offers significant advantages over traditional techniques including grafting. The reducing opposed multilobed flap involves a series of semicircular lobes extending both cephalic and caudal from the defect. The technique involves lobes most distant from the primary defect being transposed in turn closer to the defect. The technique does not result in the unnecessary excision of Burrows triangle skin. The reducing opposed multilobed (ROM) flap reduces skin tension concerns, lowers the risk of flap necrosis and allows for quicker and more aesthetic healing.

After 20 cases, we have yet to experience dehiscence, infection or delayed healing. The healing wound is resistant to contraction and invariably produces an acceptable aesthetic outcome.

The ROM flap repair allows the dermatologic surgeon an additional option when faced with a medium sized lower leg defect following skin cancer excision.

**Introduction:**

Surgical defects on the low leg following excision of skin tumors are often problematic. The skin can be tight, especially anteriorly. Skin can be thin and of poor quality. Medical conditions such as peripheral vascular disease and diabetes can further compromise prospects of wound healing.

Traditionally small (< 10mm) defects on the low calf are closed by direct closure. Larger defects are traditionally closed by split skin graft.[163]

There has been much attention to defects between 10 and 35 mm in diameter. To avoid the need for a split skin graft, a number of techniques have been popularized for these medium sized defects.

We describe a new random pattern flap technique for closing elective intermediate low leg skin defects. The reducing opposed multilobed flap (ROM Flap) addresses many of the shortfalls of previous skin closures of this size in this region. Replacing graft closure with a random-pattern flap repair enables the dermatologic surgeon to handle some low limb skin tumors in their own surgery that might otherwise require hospitalization.

Background:

Following excision of a skin tumor from the low calf, the elective defect remaining can be difficult to address. There is often minimal adjacent skin available for closure. Blood supply can be poor. The older populations that often suffer non melanoma skin cancer in this region are even more likely to have skin of poor quality and reduced perfusion.

Primary closure is limited on the lower leg to small defects. Even 10 mm diameter defects cannot always be closed directly. Skin tension can remain excessive and wound breakdown is relatively common. In addition, closing such defects with an ellipse means that skin at each of the tapered ends of the ellipse is “wasted”. That is, skin is removed beyond that required for adequate margin clearance of the tumor. In a patient with tight skin and considerable prospects of additional skin tumors elsewhere on the low leg, such skin wastage is not in the patient’s interests.

Random pattern flaps have been tried on the lower leg with limited success. Random pattern flaps can minimize skin “wastage”. However, skin tension can remain excessive for optimal healing. Excessive skin tension in closing a skin flap predisposes the flap to partial necrosis, usually to the extremity of the flap.

Furthermore, the length to base ratio of most random pattern flaps is such that perfusion to the tip of the flap becomes even more questionable. For example, a rhombic transposition flap has a length to base ratio of 1:1. The distal segment of this popular flap often lacks perfusion in usage on the lower leg, especially if the patient is elderly. A random pattern flap to the low leg needs to have a very favorable length to base ratio to ensure an acceptably low risk of end flap necrosis.

Other techniques for managing medium sized low leg defects include allowing the wound to heal by second intention. This approach has a role in some patients, but is invariably slow and involves considerable time with leg elevation. Furthermore, substantial nursing care and attention is required through the wound healing process. Others manage these types of defects with a purse string suture encompassing the entire defect. This often reduces the size of the defect to heal by second intention.

Surgical technique:

The diameter of the elective defect is measured. A mark is placed at the most cephalic aspect of the defect. From this point, a semicircle is drawn with a diameter 60 % of the diameter of the defect. A semicircle the same size is then drawn at the caudal end of the defect. The caudal semicircle must be orientated in the opposite direction to the cephalic semicircle. (See Figure 1)

Two more semicircles are drawn at the cephalic and caudal aspects of the original semicircles. These semicircles are 60 % of the diameter of the first semicircle. Additional semicircles are repeated, each being 60% the diameter of the preceding semicircle until the diameter of such semicircles measures 5 – 8 mm in diameter. (Figure 2)

Incisions are made along the semicircular surgical markings. The skin is then undermined in all directions. (Figure 3).

Starting at the extremities of the wound, the smallest semicircular flap is transposed into the adjacent larger semicircular defect. The suture is placed in keeping with the cross markers in Figure 1. The result is demonstrated in Figure 4.

The next semicircle flap is then transposed into its adjacent larger defect and sutured as indicated by the star markers in figure 1. Figure 5 demonstrates the closure at the completion of this stage. This process continues until the two largest semicircular flaps are transposed into the primary defect. (Figure 6).

This suturing process to this point may require deep anchor sutures at the locations identified in Figure 1. In our experience this is not often necessary. Skin hooks are helpful in positioning the lobes for deep and superficial suturing.

The semicircles transposed into the primary defects are then sutured in place as shown in Figures 6-8.

Additional sutures are then placed in the smaller transposed flaps to ensure wound edges are suitably approximated. (Figure 7 and 8). Figure 9 shows the completed repair. In this case the wound is on the antero-medial aspect of the right low leg and follows resection of an invasive squamous cell carcinoma.

Why 60%? We undertook modeling using a spring tension gauge on skin hooks. If the lobes were all reduced by 55%, the tension borne by the centre of the repair was significantly higher than the tension borne at the ends (peripheral tension).

With 70% reducing lobes, the peripheral tension was excessive compared with central tension. We attempted to find reducing lobes that enabled tension to be assumed evenly through the wound. Sixty percent produced even tension. Sixty-five percent reducing lobes produced slightly greater peripheral to central tension.

This crude modeling with the gauge on skin hooks was then applied to patients and their defects. In clinical application, the 60 % principle held up well. Some additional refinement of this model may produce further improvements in this technique.

We also tried models with variable percentage reductions. This increased the complexity of the overall repair without apparent improvement in the distribution of tension through the wound.

By way of comparison, primary elliptical closure, by its very nature, involves maximum wound tension centrally with very low wound tension peripherally. This places the centre of a tightly closed ellipse at considerable dehiscence risk.

The ROM flap can be applied to defects resulting from Mohs micrographic surgery or from defects based on a clinical margin of normal skin. We recommend that the specimen is marked to indicate its most cephalic point. We prefer use of a suture marker at this point. This allows easy correlation between the specimen and the wound should any revision be required. (Figure 9)

Post operative care:

Our patients are generally advised to restrict walking for two days to meet essential needs. From that point onward, we allow a gradual increase in walking capacity. We advise elevation of the leg when seated or lying. We do not require patients to spend lengthy periods with strict elevation. Most

patients have returned to full duties by day 4, - except that we continue to ask them to elevate the leg when seated.

Figure 10 shows the same wound seven days following repair. Note that the semicircular incision loops have considerably lengthened and now appear as lines with waves either side of the wound centre. This effect is similar to a "Z" plasty effect. The wound is lengthened and subsequent contracture risk is reduced. The "Z" effect also allows tension in the healing to be assumed in multiple planes, reducing the risk of sudden tension in the plane perpendicular to the principle wound axis causing dehiscence.

All wounds have an occlusive dressing applied following surgery. We ask patients to leave this dressing intact for at least 4 days. We review the patient after one week and apply a further occlusive dressing. We review patients a week later for removal of sutures. Figure 11 shows the same wound eighteen days following repair. Healing is progressing. Figure 12 shows the wound one month after surgery.

Discussion:

A number of techniques have been tested to allow medium sized low leg defects to be closed satisfactorily without the need for a graft. Blair et al.[164] describe how a long established technique involving opposing island pedicle advancement flaps can be applied to this clinical scenario. Delayed healing and wound infection still affected 15% of cases studied. Local subcutaneous flaps without an axial blood supply can produce poor perfusion compared with random pattern flaps. Penington et al[86] describe a variation on this technique whereby a single "V" - "Y" advancement flap is effected rather than two flaps. Delayed healing and partial flap necrosis remain issues with this technique.

The risk of partial flap necrosis can be reduced by shortening the distance of the random pattern of vasculature to the end of the flap. The ROM flap involves a very favorable length to base ratio of approximately 0.5:1. (Figure 13)

Complex axial flaps have proved successful in numerous lower leg deficits.[165, 166] These flaps involve mobilizing skin and deeper structures on a neurovascular pedicle. In particular, trauma that results in loss of much deep tissue as well as skin can be closed with good results using microvascular flaps, often based on the saphenous or sural systems. Most skin cancer deficits, however, on the lower leg involve only a skin defect along with subcutaneous tissue. Deeper structures are less commonly resected. With muscle planes and structures intact, disrupting same to close a skin defect is rarely appropriate.

Bilobed flaps were initially popularized for nasal defects following excision of non melanoma skin cancer. Indeed this technique has considerable advantages for nasal repairs.[128, 167] A bilobed flap allows excess skin around the bridge of the nose to be transposed through two lobes to a lower nasal defect.

Bilobed flaps have more recently been used as a means of closure for elective lower leg deficits. Bilobed flaps traditionally involve minimal if any reduction in lobe diameter as the flap is affected. As such, this technique can displace the wound tension when applied to the leg rather than spread the wound tension throughout the repair.

The bilobed concept and the axial flap concept have also been combined regarding large lower leg defects[168]. This technique is perhaps more relevant to very large defects or defects involving much deeper structures than the medium sized defect resulting from skin cancer excision from the lower calf. "A" – "T" type and "O" – "Z" type flap repairs have also been used to close low leg defects.

Motley et al[169] describes an alternate method of adapting an established random pattern flap technique for usage on the lower leg. This involves meshing an advancement flap. This useful technique can result in the unsightly "fish scale" effect that follows skin meshing.

Cross leg flaps have also been used to close leg defects[170]. This results in prolonged incapacity and immobilization, and is suggested by the authors as being a consideration when considerable bone is exposed. This technique is not applicable to common leg defects following skin lesion excision from the leg.

**Conclusion:**

Although to date we have only performed this technique on twenty patients, we feel the reducing opposed multilobed flap repair offers another alternative when the dermatologic surgeon is faced with a medium sized defect on the low leg. To date, we have not experienced a patient suffering wound infection, flap necrosis or delayed or non-healing of their wound. Further, the dermatologic surgeon may be able to handle additional low leg cases in the surgery without the need for hospitalization.

Table 1 compares the theoretical benefits and disadvantages of the ROM flap with traditional primary closure and split skin graft for low leg defects. A larger trial is needed to compare the ROM flap closure with existing methods of closing medium sized low leg defects. The authors have commenced such a trial.

Figure 1

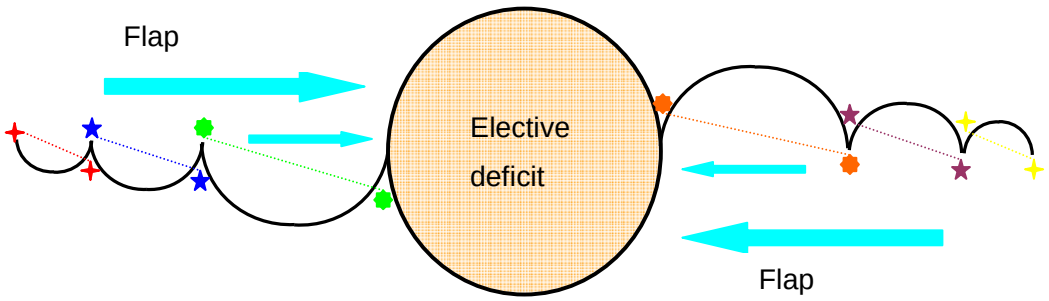

Figure 2:

Figure 3:

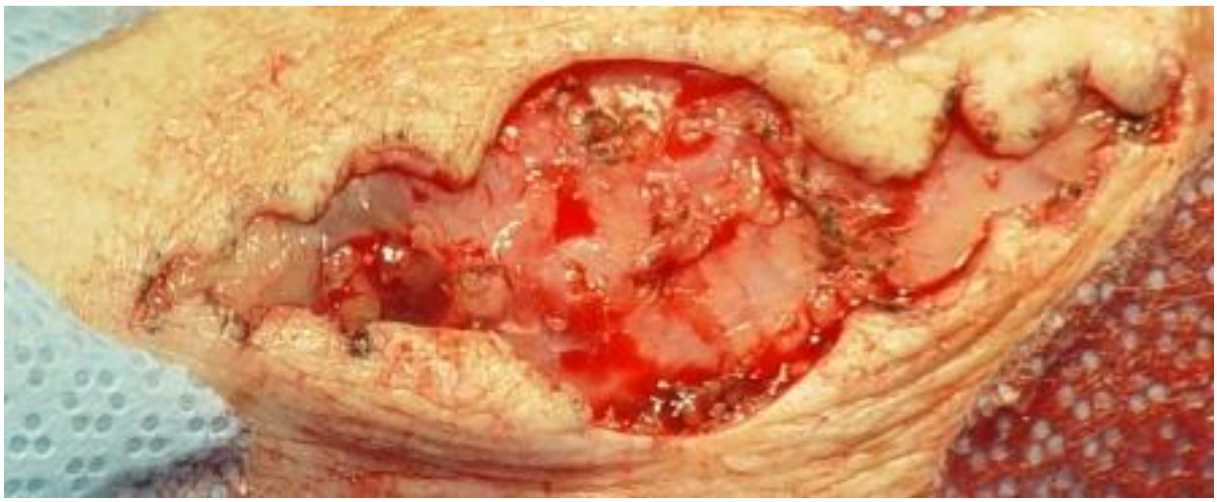

Figure 4:

Figure 5:

Figure 6:

Figure 7:

Figure 8:

Figure 9:

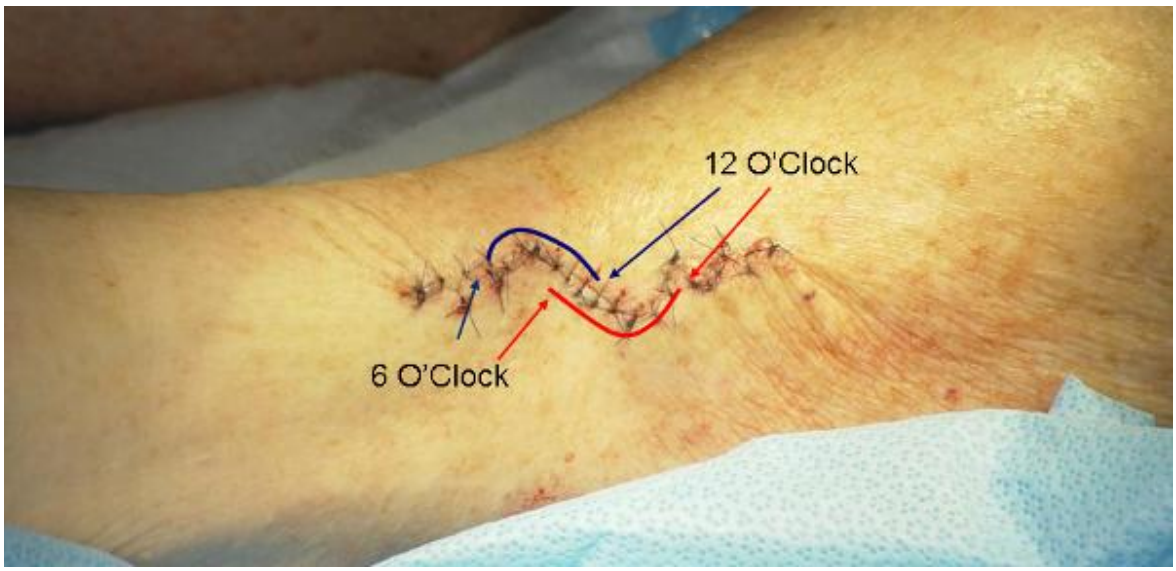

Figure 10: Seven days post operative

Figure 11:

Figure 12 One month following ROM flap repair of a defect following excision of invasive SCC from low calf

Figure 13

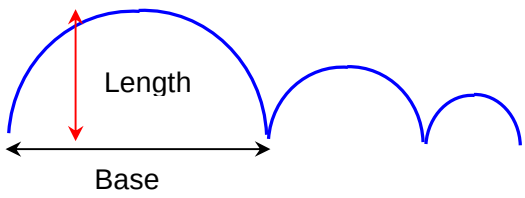

Table 1. Comparison of ROM flap to traditional techniques for closure of low leg defects.

| Feature | ROM Flap | Primary Closure | Split Skin Graft |
|---|---|---|---|
| Role closing elective medium defect size on low leg | Can often close with acceptable tension, avoiding graft | Closes small defects, medium defects close with considerable skin tension | Can be used even on very large defects |
| Difficulty of technique | Most difficult | Simplest technique | Intermediate |
| Donor site required | No | No | Yes |
| Elevation post op | 1 – 4 days | 2 – 5 days | Can be weeks |
| DVT risk through immobilization | Low | Low | High |
| Dehiscence risk closing medium sized defect | Low | High | Low |
| Cosmetic outcome | Good | Excellent if heals uneventfully, poor with breakdown or dehiscence | Poor, often depression at graft site, skin quality can be poor. Graft often has poor color and texture match |
| Return to normal duties | Quick | Slower | Slowest |
| Possible need for deep anchor sutures | Slight | High | No |
| Follows natural skin lines of tension | No | Yes | No |
| Post op care required | Average | Average | Heavy. Numerous dressings to both sites. Significant nursing care. |
| Wound length | Large for deficit | Shorter | Deficit length (& width) |
| Skin “wastage” | Minimal | Can be considerable | Minimal |
| Ease of identifying site for revision of a margin | Easy-if specimen oriented and marked | Same | Same |
| Wound tension in multiple planes | Semicircular incisions result in tension assumed in multiple planes | No, - All tension in a single plane | Graft assumes the negligible tension in wound |
| Coping with friction in post operative period | Small movement of negligible concern | Small movement of slight concern | Movement can interfere with graft taking |
| “Z” effect in repair to achieve wound lengthening and counter future wound contracture | Semicircular incisions lengthen wound in healing phase, - contracture risk greatly reduced | No lengthening possible, wound contraction can be disabling | Graft contracture risk |

## *Summary*

This chapter described the development of and design principles of the ROM flap.

The manuscript describes a theory but does not evaluate whether this theory works. The idea of the ROM flap may or may not result in legs that heal better than closures using traditional techniques.

This introductory paper describes outcomes on only 20 patients. Greater numbers and data comparing patients who have undergone a ROM flap with those closed with other techniques are needed to validate the novel technique. Chapter 4 details my retrospective data on this ROM flap technique, detailing to what extent the theoretical advantages were realized.

# Chapter 4 Reducing opposed multilobed flaps result in fewer complications than traditional repair techniques when closing medium sized defects on the leg following excision of skin tumour

Chapter 3 describes the reducing opposed multilobed (ROM) flap and the potential it has to reduce complications based on its design. It was incumbent upon me to determine whether or not this novel technique delivered on the theoretical advantages. It remained simply an idea until it was trialled.

With this in mind, we subjected the ROM flap technique to a retrospective study once the procedure had been used for twenty months. By this time I had closed 140 defects with the novel technique. To evaluate the procedure, we compared outcomes from this procedure to outcomes from other below knee procedures from the time my extensive database commenced, (July 2002).
That is, the final 15 months of closing mid-sized leg wounds with other techniques was compared to the first 20 months of ROM flap usage.
This study was a sequential series of all techniques used prior to flap development to usage of the ROM flap thereinafter. The trial was published in “Dermatologic Surgery” in July 2006[171] and the full text of the manuscript is as follows:

# Reducing opposed multilobed flaps result in fewer complications than traditional repair techniques when closing medium sized defects on the leg following excision of skin tumour.

Authors:
Dr. Anthony J. Dixon. MB,BS. FACRRM. Dip.RACOG.
Dermasurgeon & Senior Lecturer, School of Medicine, University of Queensland, Australia

Assoc. Prof. John B. Dixon, MB,BS. PhD. Dip.RACOG. FRACGP.
Assoc. Prof. Centre for Obesity Research, Monash University, Melbourne, Australia
Keywords:
Calf, shin, foot, cancer, SCC, BCC, melanoma, surgery, Mohs

**Abstract:**

Method: This retrospective study compares 140 defects closed with a reducing opposed multilobed (ROM)) flap[141] with 85 defects closed with traditional techniques.
Results:
A total of 225 defects between 11 and 44 mm in diameter were excised over 3 years from July 1st 2002.
There were 140 defects closed by ROM flap and 85 non ROM closures including 29 “O-to-Z” flaps and 12 bilateral transposition flaps. A total of 111 squamous cell carcinomas, 64 basal cell carcinomas, and 11 melanoma were excised.
ROM flap closures developed 20 complications (14.3%) 13 infections, 5 partial wound dehiscence, and 2 partial end flap necrosis.
Non-ROM closures developed 27 complications (31.8%):13 infections, 6 partial end flap necrosis, 4 partial dehiscence, 2 wound depression, 1 hemorrhage, and 1 persisting pain. Three ROM and 7 non-ROM cases suffered two complications.
The total complication rate was significantly lower with ROM flaps (P=.003), including lower end flap necrosis incidence. (P=.027)
Conclusion:
The ROM flap results in fewer complications than traditional techniques when closing defects 11 to 45 mm in size on the leg and foot. In particular, end flap necrosis incidence is lower with ROM flap closure.

**Introduction:**

Managing skin cancers below the knee poses special problems for the surgeon. Wounds heal poorly compared with other skin sites on the body. Skin is often tight, especially on the shin, limiting its mobilization to close an adjacent defect. Circulation is often reduced or poor. Infection rates can be higher than elsewhere on the body.

Small defects (less than 11 mm in diameter) are usually able to be closed directly. Larger wounds

become increasingly difficult to close directly due to skin tension.

Skin grafts can be used to close large leg wounds. Grafts do not suffer the tension issues faced with direct closure. However, grafts have their own difficulties, including failure to take and poor aesthetic outcomes. Wound depression is so common in skin graft closures that it is almost an expectation. Further, skin grafts on the leg require considerable periods of elevation and immobilization and the associated health risks such as deep venous thrombosis (DVT). Nevertheless, Skin grafts remain the most common realistic closure technique for large leg defects, (> 45 mm diameter).[163]

But what of medium sized defects, 11 – 45 mm in diameter? These defects are often too large to close directly, yet it would be disappointing to subject the patient to a graft for a defect of this size.

Many random pattern skin flaps such as rotation, advancement, transposition and island pedicle flaps have been used for these medium sized defects[163, 164, 172]. Bilobed type random pattern skin flaps, though initially described for nose defects[128, 167], have found usage elsewhere including below the knee. End flap necrosis rates can be high, however, with delayed healing and wound breakdown common. Patients may spend lengthy periods before returning to normal ambulation and activity.

Other techniques including cross leg[170] and meshed[169] flap techniques have been described, but have significant functional and / or aesthetic disadvantages for the patient and may be more appropriate for larger defects.

Axial, fascio-cutaneous and related flaps remain an option for large defects but have the disadvantage that subcutaneous sheath and tissues are incised and mobilized[86, 166, 168, 173, 174]. These flaps are also predominantly for usage in other circumstances and for larger defects.

Defects can be left to heal by second intention. This often results in lengthy periods of leg elevation as well as delays in returning to normal ambulation and activity. Further, patients with wounds healing by second intention can suffer non healing and chronic ulceration problems.

The reducing opposed multilobed (ROM) flap[141] was developed from first principles to attempt to address the traditional problems associated with random pattern skin flaps and second intention healing below the knee. (Figure 1) Using the ROM technique, all skin flaps have a low Length –to-Base ratio of 0.5. (Figure 2) Further, there are no “up-hill” flaps involved in this closure where the base of the flap is distal to the end of the flap. For these reasons the end flap necrosis rate and wound breakdown risk should be reduced when below knee defects are closed using this technique.

Skin “wastage” is also an issue in below knee defect closures. An elliptical closure can result in up to twice as much skin being excised as would be required for excising the lesion with an appropriate margin alone. If several skin lesions are excised, then the increasing loss of otherwise normal skin

compounds the patient's ongoing skin loss problems.

The ROM flap technique involves no skin wastage while enabling the patient to mobilize the same day as the surgery. While the theoretical benefits of the ROM flap are encouraging, evidence is needed to identify whether this translates into benefits for the patient.

The aim of the retrospective analysis was to ascertain whether theoretical benefits from the usage of the ROM flap below the knee were borne out by improved outcomes and fewer complications.

**Method:**

We retrospectively analyzed all patients treated at a dedicated skin cancer surgery unit over three years between July 1st 2002 and June 30th 2005.
We excluded all tumours managed by non surgical means. Only lesions excised and defects closed with suture were included. We also excluded any defect smaller than 11mm in size or larger than 45 mm in size. All skin sites below the knee were included. This includes the foot.

There were no exclusions based on medical conditions, including diabetes, peripheral vascular disease, peripheral neuropathy, Alzheimer's disease and peripheral edema. Further, a tight or inflamed skin character did not lead to exclusion.

The age and sex of each patient was noted as well as whether they were diabetic, a smoker or were on anticoagulant therapy. In keeping with recommended practice[175], anticoagulants would not be ceased other than in the event that INR levels were over the therapeutic range.

The retrospective study involved consecutive sequential series of patients. Non ROM techniques were used from July 2002 until October 2003. With the introduction of the ROM technique in October 2003, all medium sized defects were then closed with ROM flaps. The change of practice in October 2003 followed frustration with complication rates from existing techniques and the identification of significant theoretical advantages with the ROM technique. Other than the change in closure technique, no other change in management was implemented. Post operative antibiotics were only given if infection was apparent. Preparation and dressing protocols were consistent throughout. No patient received preoperative prophylactic antibiotics.

The ROM technique has been described previously by us[141]. Briefly it involves a series of semicircles extending strictly in a cephalic and caudal direction from the primary defect, (Figure 3). Semi circles closest to the defect are 65% of the diameter of the primary defect. Each subsequent semi circle is 65% of the diameter of the previous semicircle. The process of reducing semi circles continues until a 5 to 8 mm semicircle is planned.

The technique involves a series of transpositions. The outer smallest semi circles are transposed into the adjoining semicircular defect. This process continues until the largest semi circular flaps are joined together to close the central defect. The

resulting wound appears as a "zig-zag" type line running cephalo-caudal down the leg. (Figure 4)

All surgery was undertaken by one surgeon. All wounds were closed with polyamide interrupted cutaneous sutures. No wound closures involved deep, subcutaneous or intradermal suturing. While such deep sutures can be useful in approximating skin edges, they are not the usual practice of this surgeon when closing defects below the knee. Surgery was undertaken with sterile gloves, equipment and drapes. The surgeon wore mask and gown. All wounds were occlusively dressed post suturing. A follow up of at least 4 weeks was undertaken on every case by consultation with the surgeon. They were also followed up by phone by nursing staff. Alternate sutures were removed two weeks after surgery with the remaining sutures removed five to seven days later.

All ROM patients were allowed to walk the same day as surgery but were asked to minimize walking for the first 24 hours following surgery. They were then progressively allowed to increase ambulation. When seated over the first three days following surgery, patients were encouraged to elevate legs where possible.

All non ROM closure patients were asked to avoid any walking for 2 days and were then advised to slowly return to normal ambulation. Skin graft patients were further advised to elevate their leg for at least 7 days where possible.

In the event that a wound dehisced or broke down, healing by second intent was effected, with minimal debridement undertaken when appropriate. All complications were assessed and recorded. Analysis was on an intention to treat basis.

All complications noted at any stage were recorded. Specifically, infection, haemorrhage, pain, dehiscence, end flap necrosis, oedema, delayed wound healing, chronic ulceration, elevation, depression, contour distortion, etc were all specifically assessed in the convalescence period.
Infection was assessed clinically based on finding three out of the following four clinical measures ; induration, erythema, pain and discharge. Any patient experiencing wound pain three months following surgery was deemed to have persistent pain.

Statistical methods:
We calculated that we needed at least 74 cases and controls in order to have a power of 0.8 to detect a reduction in the complication rate by 50% from 40% to 20% with a p value of $< .05$
Descriptive statistics regarding subjects were presented as mean values. Differences in proportions of complications between groups were assessed using Chi square test.

**Results:**

A total of 417 below knee post excision closures were effected on below knee wounds in the skin cancer surgery centre from July 1$^{st}$ 2002 until June 30$^{th}$ 2005. No tumor required excision of tissue beyond fat and surrounding subcuticular soft tissue structures.

A total of 189 defects were below 11 mm in size and were closed directly. Three defects were more than 45 mm in size and were closed with partial thickness skin grafts.

A total of 225 defects were medium in size (between 11 and 45 mm in diameter) and were hence included in this analysis. The diagnoses managed to produce these 225 defects are detailed in Table 1.
A total of 111 were squamous cell carcinoma and 64 were basal cell carcinomata.

A total of 140 medium sized defects were repaired with ROM flaps. Of these, 135 defects were fully closed while the remaining five defects were reduced in size by at least 80% by incompletely closed ROM flaps. Two of these residual defects had a graft applied. Three residual defects were left to heal by second intent. The largest size of the five residual defects was 13 x 12 mm in size. These five cases were included with the other ROM flaps in analysis on an intention to treat basis.

Eighty-five medium sized defects were closed with procedures other than the ROM flap. Twenty-two of these defects were closed directly. Sixty-one defects were closed with random pattern skin flaps that were not ROM flaps. Twenty-nine of these flaps were "O to Z" type closures. Six defects were closed with simple transposition flap repairs. Twelve defects were closed with bilateral transposition flap repair. An additional six defects were closed with bilobed type transposition flap repairs. The remaining 8 random flap closures were; 1 "A to T" repair, 2 rhombic transposition repairs, 2 simple rotation flaps, 1 "V to Y" type island advancement flap and 1 triple transposition flap repair.

There were no significant differences in the characteristics of the two groups of patients. ROM flap patients had a mean age of 58.0 years compared with non ROM patients whose age was 59.8 years on average. There were 104 defects on men and 121 defects on women included in the study. Nine per cent of patients were on Warfarin therapy while 24% were on Aspirin therapy. Fourteen per cent of patients were diabetic and 15% of patients were smokers.

The range of defects closed with ROM flaps varied from 11 to 44 mm in diameter. Defects closed by other techniques varied from 11 to 31 mm in diameter. There were no defects between 31 and 45 mm in this study until the ROM technique was being used.

This is a consecutive series. All non ROM closures were undertaken between July 1$^{st}$ 2002 and October 2003. All ROM flap closures were undertaken between October 2003 and June 30$^{th}$ 2005.

In both groups wounds that suffered infection, wound dehiscence or end flap necrosis were allowed to heal by second intent. No wound underwent flap / scar revision.

Two defects were electively closed with split skin grafts. Both of these developed wound infections.

As there were few split skin grafts and as graft outcomes are known to be different to closures where skin edges retain their blood supply at closure, the skin grafts were excluded from further analysis.

Complications experienced (Table 2)
A total of 140 ROM flap closures experienced 20 complications in 17 closures. Three ROM closures suffered both infection and partial wound dehiscence.

Eighty-three non ROM closures (closed either directly or by non ROM random pattern flaps) experienced 24 complications in 18 closures. Six non ROM closures suffered two complications.

Partial end flap necrosis was low in the ROM group with only two cases experienced (1.4%). In contrast, six non ROM closures suffered partial end flap necrosis, (7.2%). This difference was significant. (p = 0.024)

Post operative infection was experienced in 13 ROM cases, (9.3%) versus 11 non ROM closures, (13.3%) p=0.36

All but one of the wound infections resolved with oral Dicloxacillin 500mg four times daily. One ROM flap wound infection did not respond to Dicloxacillin but responded subsequently to Ciprofloxacin 750 mg twice daily for 10 days.

Partial wound dehiscence was experienced in five ROM cases (3.6%) versus four non ROM cases (4.8%) This difference was not significant (p=.65). No dehiscence extended the full length of the wound.

While post operative infection and dehiscence rates were not significantly different, the trend favored ROM flap repairs. This contributed to an overall complication rate of 20 (14.3%) in ROM cases and 24 (28.9%) in non ROM cases. This difference is highly significant. (p=.008)

Seventeen ROM wounds suffered one or more complications, (12.1%). In contrast, 18 non ROM wounds suffered one or more complications (21.7%). (p=.06)

We effected a sub-analysis of “O – Z” repairs given they were the most common of the non ROM techniques used in this series. The 29 cases closed with “O – Z” type flap repairs suffered a total of 7 complications (24.1%). These were two infections, three cases of end flap necrosis, one persistent pain and one wound dehiscence. Although “O – Z” closures suffered a lesser percentage of complications than the other non ROM flaps, the difference was not significant, (p=0.25).

There was no case of intra-operative bleed beyond 100ml and no case of postoperative bleed in those patients continuing to take anticoagulants. No patient had a pre-operative INR in excess of therapeutic range. As such, none of the 72 patient taking Warfarin and / or aspirin discontinued their medication. There was no case of lymphoedema experienced.

All ROM patients tolerated the procedure well, with no patient expressing concern or disapproval with their surgery. In contrast one patient following skin graft, one patient following bilateral transposition repair and one patient following "O – Z" repair complained of the slow healing and length of time to return to full mobilization. All ROM patients had excellent final cosmetic outcomes, including the five cases that did not fully close with the ROM technique alone. There was no ROM closure that resulted in an unsightly scar, wound depression or elevation.

**Discussion:**

Patients with defects closed with ROM flaps suffered significantly fewer complications while walking early post surgery, - the same day.

The theoretical modeling of the ROM flap suggested wounds would have less tension, increased end flap perfusion, and quicker healing. This expectation of the ROM flap, with its low length-to-base ratio and lack of "up-hill" flaps was borne out by the significant reduction in the incidence of end flap necrosis in ROM patients.

Although the trend for ROM patients having lower infection and other complications did not reach statistical significance, they contributed to the overall significantly lower complication rate experienced by ROM patients.

ROM flaps were used to manage larger defects than the non ROM group. The largest ROM defect was 44 mm compared with 31 mm in the non ROM group. The apparent ROM procedure advantage is perhaps further supported by its better results despite this larger defect size range. The ROM procedure was well tolerated with excellent patient acceptance.

As no bleeding complications were experienced in any patient, the policy of not ceasing anticoagulants for this type of surgery is supported. Reduced ambulation following surgery below the knee places patients at increased risk of DVT. Continuing anticoagulant prophylaxis / therapy minimizes such DVT risk.

While no case of DVT was experienced in this series, the early mobilization of patients following ROM closure should theoretically further reduce risk of this complication. A much larger study would be required to identify whether this theoretical reduced DVT risk is realized.

This study has some significant limitations. There was no randomization. This consecutive series involved only one surgeon. As a consecutive series, there is the possibility that improved experience for both surgeon and nursing staff contributed to the better outcomes of ROM cases. As a new procedure, however, the surgeon had no experience with ROM flaps before this study. Further, the surgeon had considerable experience before the first excision in this trial, having excised and closed over 8000 skin lesions prior to the commencement of this study. There were several nursing staff changes over the study period. At all times during the study both, experienced and inexperienced nursing staff was

involved in patient management. Although most patients were followed up for many months, not all were available for longer term follow up.

Not all skin cancers below the knee require surgical excision to manage the tumor. Other treatments include; curette (with or without electrodessication), imiquimod ointment, photodynamic therapy and cryotherapy. Further, clinicians can leave post excision wounds to heal by second intention following excision of tumor. Second intent healing can produce excellent results for defects below the knee, but recovery time and time spent with leg elevation can be considerable, with the subsequent disadvantages to patient. ROM flaps enable prompt return to walking and normal activity.

**Conclusion:**

Patients with medium sized defects (11 – 45 mm) below the knees closed with a ROM flap experienced significantly fewer complications than patients with the similar sized defects closed by other means.

In this consecutive series study, end flap necrosis rates were also significantly lower in defects closed with ROM flap versus those closed with other techniques.

Although this study is not randomized, it demonstrates that in the hands of this surgeon, defects below the knee between 11 and 45 mm in size should be closed with a ROM flap hereinafter.

Dermasurgeons should consider adopting this technique.

A future prospective random control trial by other surgeons would further evaluate the role of the ROM flap in closing medium sized elective defects on the leg and foot after skin lesion excision.

Table 1:Diagnoses of all lesions excised producing defects 11 to 45 mm in diameter.

| Diagnosis | Number | Percentage |
|---|---|---|
| Invasive SCC | 79 | 35.1 |
| Nodular / Invasive BCC | 38 | 16.9 |
| SCC in situ (Bowens Disease) | 32 | 14.2 |
| Superficial BCC | 26 | 11.6 |
| Keratoacanthoma | 12 | 5.3 |
| Invasive malignant melanoma | 10 | 4.4 |
| Lentigo maligna melanoma | 1 | 0.4 |
| Hyperkeratotic actinic keratosis | 10 | 4.4 |
| Other benign lesions | 17 | 7.6 |
| TOTAL | 225 | 100 |

SCC = squamous cell carcinoma; BCC = basal cell carcinoma.

Table 2: Complications experienced with various closures (excluding 2 split skin grafts)

| Type of wound closure | Infection | Partial Dehiscence | Other complications | Total |
|---|---|---|---|---|
| ROM flap (N = 140)** | 13 (9.3%) | 5 (3.6%) | 2 (central flap necrosis) (1.4%) | 20 (14.3%) |
| Ellipse & close direct (N = 22) (Non ROM) | 3 (13.6%) | 1 (4.5%) | 1 (wound depression) | 5 (22.7%) |
| Other skin flap (N = 61) (Non ROM) | 8 (13.1%) | 3 (4.9%) | 8 in total comprising<br>• 6 flap necrosis<br>• 1 persistent pain<br>• 1 post operative bleed | 19 (31.1%) |
| Total Non ROM closures (N = 83) | 11 (13.3%) | 4 (4.8%) | 9 (10.8%) | 24 (28.9%) |
| TOTAL (N=223) | 24 (10.8%) | 9 (4%) | 11 (4.9%) | 44 (19.7%) |

** 5 ROM flaps did not close completely, leaving residual defect up to 20% of original size

Figure 1: The layout for the reducing opposed multilobed (ROM) flap repair.

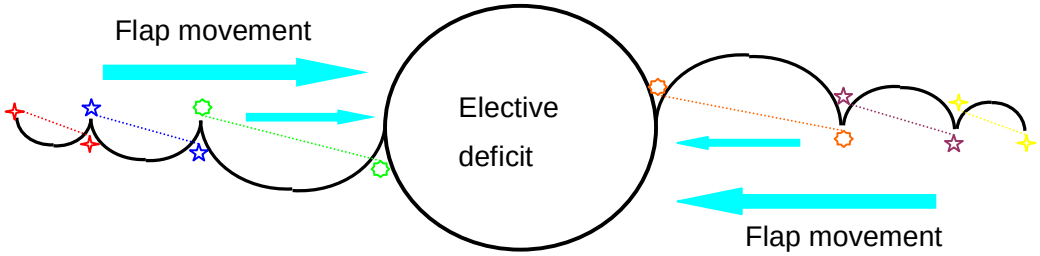


Figure 2 : Being a semicircle, the length to base ratio of ROM flap is 0.5

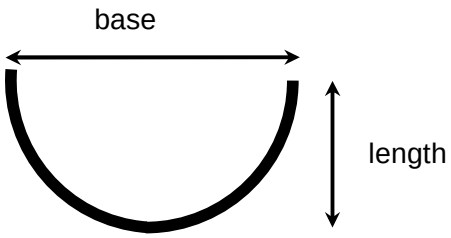


Figure 3: Larger ROM flap layout demonstrating no “up hill” flaps.

Figure 4: Following surgery as planned in Figure 3

## *Summary*

This manuscript describes the extent to which the ROM flap delivered on its potential to reduce complications following skin cancer surgery below the knee. Chapter 1 identified that infection incidence is higher below the knee. Chapter 2 revealed that mupirocin ointment did not lower this risk. Chapter 3 and 4 identified that while the ROM flap assisted other outcomes, no improvement in the infection incidence was identified.

While the ROM flap did not reduce the incidence of wound infection to statistical significance, the technique did result in reduced incidence of flap necrosis, and overall complication incidence. This trial helps validate the ROM flap technique for usage closing defects below the knee from 11 to 45 mm in diameter.

This study was retrospective, - the only retrospective study in this suite of studies for PhD by publication. This is a major limitation of this study. A randomized controlled trial would remain useful in the future to validate further the ROM flap technique.

There was but one case of post operative bleeding noticed in this entire below knee wound trial, (0.4%). This contrasts with post operative bleed incidences reported on the literature of around 3%.[51] This raises the question as to whether the leg is a region of unusually low post operative haemorrhage risk or whether our overall incidence of bleeding was lower than suggested figures. This question could be answered through my concomitant prospective study of bleeding complications, a study that had been in progress since my database commenced.

The next chapter describes the first of my two bleeding studies. They focus primarily on the issues surrounding patients taking warfarin and aspirin medication at the time of their skin surgery. We planned to identify when and whether an increased bleeding incidence might eventuate such that temporary ceasing of warfarin and / or aspirin may be advisable.

# Chapter 5 Bleeding complications in skin cancer surgery are associated with warfarin but not aspirin therapy – a prospective study

Chapters 1 and 2 pertain to the issue of infection complications following skin surgery. Chapters 3 and 4 deal with the ROM flap and how it can result in reduced skin surgery complications. Now we change focus from an emphasis on infection to post operative bleeding complications following skin cancer surgery. Such is the subject of chapters 5 and 6. These studies were designed to address some of the other questions that had arisen concerning bleeding complications.

- Should patients cease warfarin for skin surgery?
- Should aspirin be ceased?
- Do some body regions bleed more than others?
- Does the technique to close the wound alter the post operative bleeding risk?
- Does gender or age alter bleeding risk?

From the outset of my randomized controlled trial of ointments[125], my approved protocol included the regarded policy that warfarin and aspirin should not be ceased for skin surgery unless the INR is over 3.0.[140, 176]

Our prospective study of bleeding complications was designed to address some of these questions. The full manuscript as published in British Journal of Surgery[177] is as follows:

# Bleeding complications in skin cancer surgery are associated with warfarin but not aspirin therapy

Authors:
Anthony J. Dixon[1], MBBS FACRRM
Mary P. Dixon[2], B Appl Sci (Nursing)
John B. Dixon[3], MBBS FRACGP PhD

[1] Director of Research, Skin Alert Skin Cancer Clinics, Australia
[2] Nurse Manager, Skincanceronly, Geelong, Australia
[3] Associate Professor, Head of Clinical Research CORE, Monash University, Melbourne, Australia.

**Abstract:**

Method:

This was a prospective study of 5950 skin lesions excised on 2394 patients. No patient stopped taking aspirin or warfarin unless the international normalized ratio (INR) exceeded 3.0.

Objective:

The aim was to identify risk factors for post operative bleeding following skin cancer surgery.

Results: The rate of post operative bleeding was 0.7 per cent overall and 2.5 per cent in the 320 patients taking warfarin. The rate of bleeding was 1.0 per cent for skin flap repairs, 0.4 per cent for simple excision and closure, and 5.0 per cent for skin grafts.

Diabetic patients and smokers were not at increased risk of bleeding. There were four independent risk factors for bleeding: age 67 years or older, odds ratio (OR) 4.7 (95per cent confidence interval, 1.8 to 12.2); *P*=0.002, warfarin therapy (OR 2.9, (1.4 to 6.3); *P*=0.006), surgery on or around the ear (OR 2.6 (1.2 to 5.7); *P*=0.012) and closure with a skin flap or graft (OR 2.7 (1.4 – 5.3); *P*=0.004). Aspirin therapy was not an independent risk factor for bleeding.

Conclusion: Warfarin therapy, increasing age, surgery on or around the ear and closure with flap or graft are independent risk factors for post operative bleeding complications in skin cancer surgery. Most postoperative bleeds were inconvenient but not life threatening, unlike the potential risk of thromboembolism after stopping warfarin or aspirin. There was no case for discontinuing aspirin before skin surgery, but the INR should be monitored in patients taking warfarin.

**Introduction:**

Some patients who require minor surgery for skin cancer will be taking antithrombotic medication such as aspirin or warfarin. Their management varies greatly from surgeon to surgeon; some routinely stop these drugs before surgery, whereas others continue them.[178]

Several studies have reported no increased risk of bleeding associated with continuing warfarin or aspirin. All but one of these studies were very small, with fewer than 100 patients on aspirin or non steroidal anti-inflammatory (NSAID) and up to 16

patients on warfarin[74, 179-181]. The largest involved 286 patients taking aspirin or NSAIDs and 26 taking warfarin[176]. The power of these studies would have only allowed the detection of a large difference in bleeding risk and would have been limited by other confounding risk factors. Bleeding is the commonest complication of skin surgery (incidence of 3 per cent), and use of anticoagulants or immunosuppressant drugs is a risk factor.[51]

In recent years surgeons have been encouraged to continue warfarin and / or aspirin therapy before excision of skin tumours[140, 176, 180-187], accepting an international normalized ratio (INR) of up to 3.5.[183] Stopping antithrombotic drugs risks life threatening thromboembolic sequelae, even when medication is stopped only for a short period. [175, 178, 188, 189].

Other forms of surgery have some data available to guide surgeons in their decision whether or not to stop antithrombotic medication. There is mixed advice regarding continuing warfarin and aspirin in patients having ocular surgery[190, 191]. Safe continuation of antithrombotics has been reported for dental[192], prostate[193] and cardiac surgery[194].

The aim of this prospective study was to monitor bleeding complications in a referral based skin cancer centre, and to identify risk factors for this complication.

**Method:**

This study involved patients managed from 1 July 2002 to 28 February 2006 at a skin cancer surgery referral centre in Geelong, Australia. Patients' antithrombotic medications were not altered either before or following skin cancer surgery unless the INR was over 3.0.

Consecutive patients who were treated during the study interval were included. Surgical procedures included modified Mohs' micrographic surgery[16]; small and large excision and closure of lesions; curettage (with or without electrodessication); skin flaps; full and partial thickness skin grafts, and wedge excision surgery. Patients on warfarin therapy must have had an INR test within a week of planned surgery, usually within two days.

Patients who stopped their antithrombotic medication before surgery were excluded, as were patients with an INR above 3.0. Other exclusions were lesions managed entirely by cryotherapy patients who had more than 15 lesions treated (to avoid over representation), and partial and full thickness skin graft donor sites.

One surgeon performed all procedures. All procedures were performed under local anaesthetic. Bipolar diathermy was used to effect haemostasis where appropriate. The site of all removed lesions was recorded and specimens underwent histopathological examination. All full thickness wounds were closed with interrupted nylon skin sutures. Absorbable deep sutures were used only if layers deep to the skin required direct closure. Occlusive wound dressings were used unless patient allergy made this impractical.

In patients with multiple tumours, the main lesion was removed first and a sub analysis of first lesions excised was carried out.

Patients had follow - up at least until removal of sutures. Patients who attended elsewhere for removal of sutures were contacted by telephone.

Post operative bleeding:

Any post operative haemorrhage or haematoma was recorded. A haematoma was regarded as small (up to 5 ml), medium (5 to 50 ml) or large (over 50 ml). A haemorrhage was regarded as small (up to 25 ml), medium (25 to 100 ml), or large (over 100ml). Haemorrhage was further classified as delayed (1 to 24 hours after surgery) and late (more than 24 hours).

Statistical Analysis:

To detect an increased incidence of bleeding of 2.5 per cent compared with 1 per cent, with a sensitivity of 0.05 and a power of 0.8, it was calculated that the study would require 280 procedures on patients taking warfarin. Recruitment continued until at least 280 procedures had been performed on patients taking warfarin and 280 on patients taking aspirin.

Demographic details were presented as percentage or mean (s.d.) as appropriate. Chi-square analysis was used to test the significance of differences between proportions and categorical variables. This method was also used to assess the invariable risk of bleeding, with results presented as odds ratio with 95 per cent confidence interval.(c.i.) Multivariable analysis using binary logistic regression (forward and backward) was used to identify independent risk factors for bleeding, and odds ratio beta-coefficients with 95 per cent were recorded. Receiver - operator characteristic (ROC) curves were used to determine the age cut off value that represented the best combination of sensitivity and specificity for risk of a bleeding complication. SPSS version 14.0.2 (SPSS, Chicago, Illinois, USA) was used for all statistical analysis. $P < 0.050$ was considered statistically significant.

**Results:**

*Participants*

A total of 5950 skin lesions from 2394 patients were treated by excision or curettage in the 44 months. Twenty-four patients (29 lesions) were excluded as anticoagulant therapy was stopped before they attended. A further three patients with an INR over 3.0 were excluded. One patient had more than 15 lesions and all lesions after the 15$^{th}$ were excluded from the study.

The mean age of the patients was 64 (17) (median 67) years; with 55.3 per cent were men. The 5950 lesions managed included 3175 malignant lesions; 1436 squamous cell carcinomas (24.1 per cent), 1381 basal cell carcinomas (23.2per cent), 166 melanomas (2.8 per cent), 24 lentigo maligna (0.4 per cent) and 168 other cutaneous malignancies (2.8 per cent). The 2775 benign lesions excised comprised; 1098 benign actinic lesions (18.5 per cent), 137 dysplastic melanocytic naevi (2.3 per cent) and 1540 other benign lesions (25.9 per cent).

Twelve patients were not seen at the time of, or after, removal of sutures and were followed up through telephone contact. All others were seen by the surgeon or nursing staff.

*Post operative bleeding*

Forty bleeds were recorded (0.7 per cent) among 5950 lesions treated. There were 14 haematomas, ten small and four medium collections. Twenty-six patients had a haemorrhage recorded; there were

twenty-two delayed and four late bleeds. Fifteen of the haemorrhages were small, ten were medium and one was large.

The latter occurred 3 weeks after surgery while the patient was on warfarin therapy. Although the INR was therapeutic at the time of surgery, it rose in the following weeks to 7.4. This was the only person admitted to hospital with post operative bleeding. Management involved stopping warfarin and wound compression.

Three patients (two on warfarin) required wound exploration to control bleeding. One patient required vessel ligation and bleeding in the other two was controlled with bipolar diathermy, and compression. Two patients (neither on warfarin) had a haematoma evacuated. Bleeding complications in all other patients were managed conservatively.

*Predictors of increased risk of bleeding*

There was no difference in the bleed rate between men and women (0.7 versus 0.6 per cent respectively, p= 0.550), but those with bleeding complications were significantly older than the remainder (75 ± 9 versus 64 ± 17 years; p<0.001). ROC curve analysis demonstrated that age 67 years provided the best cut-off value for the risk of a bleeding complication.

There were six bleeds (2.1 per cent) among 285 skin cancer procedures undertaken in 67 patients receiving warfarin therapy only (Table 1). This incidence was significantly higher than in patients not on warfarin) (P<0.001). A total of 829 skin cancer procedures were undertaken on 334 patients taking regular oral aspirin. Nine instances of bleeding were documented (1.1 per cent), and the incidence was higher than in patients who were not on aspirin (p=0.032). There were two bleeds among 35 skin cancer procedures in 11 patients managed with both warfarin and aspirin. The incidence of bleeding was significantly higher than in patients not on antithrombotics, (P < 0.001).

A sub-analysis of the first procedures revealed a significantly increased rate of bleeding in those on warfarin but not those receiving aspirin, (Table 1).

The rate of bleeding after each surgical technique is summarized in Table 2. Only skin grafts were associated with a rate over 4 per cent. Bleeding was least common when wounds were closed directly, (0.4 per cent) or managed by curettage, (0.2 per cent).

Bleeding was not more frequent in diabetics (1.5 per cent; two of 135 first procedures) (P=0.86). Similarly the rate in smokers (0.4 per cent; one of 287) wasn't different (P=0.491).

Univariable analysis showed that a number of factors were associated with an increased risk of bleeding complications after surgery; age of 67 years or greater, warfarin therapy, aspirin therapy, flap or graft closure, and surgery on or near the ear, (Table 3).

Binary logistic regression revealed that aspirin was not an independent factor as older patients were more likely to take aspirin. The remaining four variables were independent predictors of bleeding complications (Table 3).

**Discussion:**

Bleeding complications were increased in patients taking warfarin, but not in those taking aspirin. There does not appear to be a case for stopping

aspirin before skin procedures. Three other independent risk factors for bleeding were age 67 years or more, surgery in the area of the ear, and flap or graft closure.

The marginal reduction in bleeding incidence risk that might be associated with stopping warfarin therapy cannot be justified uniformly when balanced against the risk of a serious thrombo-embolic event[188, 189].

This risk has been variously estimated between one in 278 and one in 11,500[175, 195]. The variation in these estimates makes it difficult to quantify the proportional risk of minor haemorrhage that a patient would suffer by stopping antithrombotic drugs.

The risk of a major thromboembolic event is estimated at 1 per cent per day if the patient has suffered a deep venous thrombosis or pulmonary embolism within one month of temporarily stopping warfarin cessation.[195]

Additional precautions to reduce the risk of bleeding may be appropriate when operating on patients taking warfarin. The INR should be at the lower end of therapeutic range, especially when several additional risk factors are present. A fixed INR recommendation cannot be made as the therapeutic range recommended for patients depends on the indication for anticoagulation.[183, 195]

There was no life threatening bleeds in this study. All were managed with relatively simple measures and bleeding complications experienced were mainly an inconvenience and did not cause significant morbidity. This contrasts with more invasive surgery. Deep cavity and organ bleeding following major surgery may be occult until substantial blood loss has occurred. In particular, abdominal and thoracic cavity bleeding can be life threatening, so the findings of this study cannot be extrapolated to major surgery.

This study has some limitations. No NSAIDS or other anticoagulants were considered. Newer antithrombotics such as ticlopidine[188] and clopidogrel were rarely being taken by patients during the design phase of this prospective study, although their usage has increased since. These recommendations regarding aspirin and warfarin cannot be extrapolated to other antithrombotics.

Table 1 Incidence of bleeding complications in patients on warfarin and aspirin

| | Warfarin therapy | Aspirin therapy | Both warfarin & aspirin therapy | Patients on neither warfarin nor aspirin | Total |
|---|---|---|---|---|---|
| Number of patients | 67 | 334 | 11 | 1982 | 2394 |
| Total no. skin cancer procedures | 285 | 829 | 35 | 4801 | 5950 |
| Total no. of bleeds | 6(2.1)* | 9(1.1)**** | 2(6)* | 23(0.5) | 40(0.7) |
| Haemorrhage | 3 | 8 | 2 | 13 | 26 |
| Haematoma | 3 | 1 | 0 | 10 | 14 |
| No. of bleeds on first procedures | 3(4)** | 2(0.6) | 1(9)*** | 14(0.7) | 20(0.8) |

Values in parentheses are percentages. *P<0.001, **P=0.002, ***P=0.003, ****P=0.032 *versus* patients receiving neither warfarin nor aspirin ($x^2$ test).

Table 2: Bleeding incidence following different skin closure techniques

| | Operations | Post operative bleeding | P * |
|---|---|---|---|
| Direct primary closure | 3364 | 14 (0.4) | 0.006 |
| Skin flap repair | 1958 | 20 (1.0) | 0.021 |
| Skin graft | 101 | 5 (5.0) | <0.001 |
| Curette | 488 | 1 (0.2) | 0.230 |
| Wedge excision and repair | 39 | 0 (0) | 0.610 |
| Total | 5950 | 40 | |

Values in parentheses are percentages. * *Versus* other closure techniques ($x^2$ test).

Table 3: Odds ratios are presented for individual factors found to be associated with bleeding and results of binary logistic regression..

| | individual factors | | | Binary logistic regression | | |
|---|---|---|---|---|---|---|
| | Odds ratio | Confidence intervals | P * | Odds ratio | Confidence intervals | P |
| Age ≥ 67 years | 7.2 | (2.8 , 18.4) | <0.001 | 4.7 | (1.8 , 12.2) | 0.002 |
| Warfarin therapy | 5.1 | (2.4 , 10.7) | <0.001 | 2.9 | (1.4 , 6.3) | 0.006 |
| Flap or graft | 4.1 | (2.1 , 7.5) | <0.001 | 2.7 | (1.4 , 5.3) | 0.004 |
| Ear surgery | 3.8 | (1.8 , 8.0) | <0.001 | 2.6 | (1.2 , 5.7) | 0.012 |
| Aspirin therapy | 2.2 | (1.1 , 4.4) | 0.026 | 1.4 | (0.69 , 2.9) | 0.349 |

Values in parentheses are 95 per cent confidence intervals. *$x^2$ test.

## *Summary*

In this study we identified four independent risk factors for bleeding in skin cancer surgery: age 67 or older, warfarin therapy, surgery on or around the ear, skin flap or skin graft closure. My results suggest that a 4% or higher incidence of post operative bleeding in skin cancer surgery is only likely in patients with three or more of the four risk factors.
Given the life threatening thrombo-embolic sequelae that can follow short term cessation of warfarin, it should not be routinely ceased for skin cancer surgery and should never be ceased within a month of a patient suffering deep venous thrombosis or pulmonary embolus.

There is a limitation in this study that again the predominant analysis was undertaken on lesions rather than patients. The independence issue arises again.

Since my trial was published, an interesting and significant study on the risks of ceasing antithrombotics was published by Garcia in the Archives of Internal Medicine.[196] The investigators aimed to assess the frequency of thromboembolism following ceasing antithrombotics. The prospective observational cohort study included 101 sites. A total of 1293 episodes of warfarin therapy interruption in 1024 individuals were included. The most common procedures were colonoscopy, oral and ophthalmic surgery. Heparin replacement was used in only 8.3% of cases overall. Seven patients (0.7%) experienced post procedure thromboembolism within 30 days. None of the 7 patients who experienced thromboembolism received heparin. 23 patients (2.2%) had post operative bleeding. 14 of these 23 received peri-procedural heparin or low-molecular-weight heparin.
The authors conclude that short term interruption of anticoagulants poses a low but statistical risk of thromboembolism.

Together with my study specific to skin surgery, the Garcia work substantially increases our knowledge of the place for ceasing warfarin short term for skin surgery.
My incidence of bleeding whilst on warfarin was 2.5%, similar to the patients in the Garcia study. Our patients may also face a thromboembolism risk in the order of 0.7% if they had their warfarin therapy interrupted. None of our patients had a serious bleed compared with 6 patients having eye, mouth or colonoscopy surgery.

Skin surgery appears to have a lower risk of serious post operative bleeds than the minor surgery studied in the Garcia trial. Given that lower risk of a serious bleed, the case for ceasing warfarin is increasingly difficult to justify for skin surgery against the possible 0.7% incidence of thromboembolism that might result from such short term medication alteration.

The other risk factors we have identified, age, closure method and location must be factors into any decision regarding short term warfarin ceasing.

Doctors managing skin lesions could benefit from more specific details of bleeding risk in all parts of the body and more details of risks faced with different surgical procedures and closures.

Further expansion of this more detailed analysis may be useful to clinicians managing skin lesions with surgery. The next chapter details the post operative bleeding incidence we identified on different regions of the body.

# Chapter 6 Skin cancer surgery to the ear risks increased bleeding complications – a prospective study

Chapter 5 gave us an overall view of risk factors for bleeding following skin surgery. Chapters 1 and 2 addressed infection complications. Chapters 3 and 4 addressed surgery below the knee. Further questions regarding bleeding complications remain.

We have demonstrated that age, more complex skin surgery and patients taking warfarin are risk factors for post operative bleeding. My earlier work did not detail sites on the body that may vary in bleeding incidence. Doctors manage skin lesions in all skin locations. Specific risks and information on individual sites can assist management decisions. Certain body locations have been considered to be at increased risk of bleeding complications. In each case the consideration is not based on substantive data. Sites on the head and neck have been considered to have an increased risk of bleeding following skin surgery.[197] Elsewhere, the ear has been said to share bleeding risk with other sites undergoing cutaneous surgery.[198]

There has been no large prospective data to assist the physician in recognizing which regions face greater or reduced bleeding complication risks. With this in mind, we compiled a prospective study of body sites and their individual bleeding complication risks. This manuscript has been published in the Journal of Plastic, Reconstructive and Aesthetic Surgery in April 2008.[199] The published study is as follows:

# Skin cancer surgery to the ear risks increased increasing bleeding complications – a prospective study

Authors:
A. Prof. Anthony J. Dixon[1], MBBS FACRRM FACSCM
Mary P. Dixon[2], B Appl Sci (Nursing)
A. Prof. John B. Dixon[3], MBBS FRACGP PhD

**Abstract:**

Method: Prospective study of 5950 skin lesions excised on 2394 patients.

Objective: To identify body sites at increased risk of post operative bleeding following skin cancer surgery procedures.

Results: Post operative bleeding incidence was 0.67% overall (40/5950). The incidence was increased at 2.16% when surgery was on or near the ear (9/416). ($p<0.001$) Bleeding incidence on the pinna was 2.24% (7/313) and the immediate post auricular incidence was 3.03% (1/33).

The only other body sites demonstrating a bleeding incidence over 1% were the nose (6/571), neck (3/199) and temple (2/137) regions. In each of these sites the increase was not significant compared to elsewhere on the body.

No bleeding complication was life threatening and most bleeds were managed with pressure and dressings. Only three patients required wound exploration to manage ongoing post operative bleeding.

Limitations: This study involved a single surgeon in Southern Australia and may not be indicative of broader skin surgical practice.

Conclusion: Postoperative bleeding following skin surgery is uncommon and is usually able to be managed conservatively. 1 in 2000 procedures might come to wound exploration due to ongoing bleeding. The ear, including immediate pre-auricular and post auricular sites are the only body regions demonstrating an increased incidence of post operative bleeding following skin cancer surgery. Attention to haemostasis during surgery and care with dressings following surgery may be more important when excisions are planned in and around the ear.

**Introduction:**

There is limited data to identify sites of skin that may be at higher risk of bleeding complications. It has been reported that surgery to the outer ear shares the bleeding risk with other parts of the body.[198] Elsewhere, ear nose and throat surgery has been identified as at higher risk of unexpected readmission with bleeding complications cited as one such reason.[200]

Aim:

Through a prospective study we identified incidence of post operative bleeding following skin surgery for all body sites to identify locations that may be at increased risk.

**Method:**

This study involved patients managed from 1 July 2002 to 28 February 2006 at the skin cancer referral centre, "Skincanceronly", Geelong, Australia. Patients' aspirin was continued and warfarin was not altered either before or following skin cancer surgery unless INR was over 3.0. In the event that post operative haemorrhage occurred, pressure, dressings and wound exploration were implemented as appropriate. This trial was approved by the Barwon Health Research and Ethics committee.

Surgical procedures included: modified[16] margin control surgery[12, 201]; direct excision and closure of lesions; curettage; skin flaps; full thickness and partial thickness skin grafts; and wedge excision surgery.

Patients were excluded if they ceased their warfarin or aspirin prior to attendance or recorded a preoperative INR level over 3.0. Bipolar diathermy and ligatures were available for all cases. All full thickness wounds were closed with nylon or polyamide interrupted skin sutures. Absorbable deep sutures were used in closure only if sheath, cartilage, muscle or other layers were breached or if dermis and epidermal closures would benefit from separate closure.

Patients were followed up at least until removal of sutures. Expanded details of the methodology have been previously published.[177]

Statistical Analysis:

Demographic details were presented as percentage or mean ± standard deviation (SD) as appropriate. Analysis was univariate (Chi-square method) and multivariate; tested using binary logistic regression (forward and backward) and odds ratio beta-coefficients with 95% confidence intervals are shown. The SPSS 14.0.2 statistical software was used for all statistical analysis. A p-value of less than 0.05 was considered statistically significant.

**Results:**

Participants

A total of 5950 skin lesions from 2394 patients were treated by excision or curettage. There were 28 exclusions. Lesions managed included 3175 malignant lesions; 1436 SCCs (24.1%), 1381 BCCs (23.2%), 166 melanoma (2.8%), 24 lentigo maligna and 168 other cutaneous malignancies (2.8%).

Post operative bleeding

40 bleeds were recorded (0.67%). There were14 haematomas and 26 haemorrhages recorded.

There was one large bleed three weeks post surgery. The patient on warfarin had a therapeutic INR at the time of surgery but it rose to 7.4 in the weeks following surgery. He was the only person hospitalized due to post operative bleeding. Management involved ceasing warfarin and wound compression.

Three patients (two on warfarin) required wound exploration to control bleeding. One patient required vessel ligation and the other two patients had bleeding controlled with bipolar diathermy, Kaltostat ® and compression dressings. Two

patients (neither on warfarin) with haematoma had their collection evacuated. All other patients had bleeding complications managed conservatively; pressure dressings and review.

*Bleeding in relation to surgical technique*

The lowest bleeding incidence was seen with wounds closed directly, (0.42%) and those managed by curettage, (0.20%)

Skin flap closure results in an increased bleeding risk, odds ratio (OR) 2.6, (1.4 – 4.9) P=0.02.

The types of skin flaps (n=1958) undertaken were; 488 transposition (24.9%), 341 bilobed (17.4%), 296 O to S (15.1%), 201 reducing opposed multilobed (ROM)[141, 171] (10.3%), 103 A to T (5.3%), 100 V – Y (5.1%), 429 others (21.9%).

Skin grafts revealed a higher risk of bleeding of OR 8.5 (3.3 – 22) P<0.001.

Bleeding in relation to site on body

The bleeding incidence at different sites on the body is detailed in Table 1.

Procedures on and around the ear showed an increased incidence of bleeding complications, 2.24% (p<0.001) Ear bleeds were greater for all procedure types or whether taking warfarin or not, (Table 2).

Surgery on the ear was combined with surgery adjacent to the ear as frequently defects on the ear were repaired with skin grafts or flaps involving adjacent skin.

No other body site demonstrated a statistical increased incidence of post operative bleeding.

Table 1: The bleeding incidence following surgery to various body regions

| | Operations | % of all sites | Post operative bleeding | Percent | P value to rest * |
|---|---|---|---|---|---|
| Head and neck | 3436 | 57.7% | 27 | 0.78% | NS P=0.23 |
| Ear | 313 | 5.3% | 7 | 2.24% | P<0.001 |
| Preauricular | 70 | 1.2% | 1 | 1.43% | NS** |
| Postauricular | 33 | 0.6% | 1 | 3.03% | NS** |
| Ear + pre & post auricular | 416 | 7.0% | 9 | 2.16% | P<0.001 |
| Nose | 571 | 9.6% | 6 | 1.05% | NS P=0.24 |
| Scalp | 327 | 5.5% | 1 | 0.31% | NS** |
| Neck | 199 | 3.3% | 3 | 1.51% | NS P=0.14 |
| Forehead | 428 | 7.2% | 3 | 0.70% | NS P=0.94 |
| Temple | 137 | 2.3% | 2 | 1.46% | NS P=0.25 |
| Cheek & Zygoma | 683 | 11.5% | 2 | 0.29% | NS P=0.20 |
| Chin & lips | 218 | 3.6% | 1 | 0.35% | NS ** |
| Eyelids | 97 | 1.6% | 0 | 0% | NS p=0.37 |
| Trunk | 1063 | 18.0% | 7 | 0.66% | NS p=0.95 |
| Back | 574 | 9.6% | 4 | 0.70% | NS p=0.93 |
| Chest | 266 | 4.5% | 2 | 0.75% | NS p=0.87 |

| | | | | | |
|---|---|---|---|---|---|
| Pectoral | 170 | 2.9% | 1 | 0.59% | NS** |
| Abdomen | 38 | 0.6% | 0 | 0% | NS p=0.58 |
| Buttock | 15 | 0.3% | 0 | 0% | NS p=0.75 |
| Lower limb | 653 | 11.0% | 3 | 0.46% | NS p=0.48 |
| Thigh and groin | 111 | 1.9% | 1 | 0.90% | NS** |
| Leg | 468 | 7.9% | 2 | 0.43% | NS p=0.50 |
| Foot | 58 | 1.0% | 0 | 0% | NS p=0.53 |
| Toes | 16 | 0.3% | 0 | 0% | NS p=0.74 |
| Upper limb | 798 | 13.4% | 3 | 0.38% | NS p=0.27 |
| Arm | 185 | 3.1% | 0 | 0% | NS p=0.26 |
| Forearm | 214 | 3.6% | 1 | 0.47% | NS** |
| Hand | 336 | 5.6% | 2 | 0.60% | NS p=0.86 |
| Fingers | 63 | 1.1% | 0 | 0% | NS p=0.52 |
| Total | 5950 | 100% | 40 | 0.67% | |

* P values determined using chi square test comparison to other body locations

** Single bleeds preclude chi square analysis

Table 2: Comparison of procedure on and near the ear with procedures elsewhere.

| Procedure | Total ear procedures# | Ear bleeds | % | Total non ear procedures | Non ear bleeds | % | P value |
|---|---|---|---|---|---|---|---|
| Ellipse | 159 | 3 | 1.9% | 3191 | 11 | 0.3 | P=0.003 |
| Graft | 65 | 4 | 6.2% | 31 | 1** | 3.2 | ** |
| Flap | 168 | 2 | 1.2% | 1770 | 18 | 1.0 | NS |
| on warfarin | 27 | 1 ** | 3.7% | 258 | 5 | 1.9 | ** |
| not on warfarin | 389 | 8 | 2.1% | 5276 | 26 | 0.5 | P<0.001 |
| | | | | 9 | | | |

Chi square analysis-**Chi square test not possible with only a single bleed.

# includes procedures on the ear as well as immediate pre and post auricular.

Table 3: The percentage of bleeding complication for patients grouped by the number of bleeding risk factors.

| | Overall bleeding rate | Percent of all cases managed |
|---|---|---|
| 0 risk factors | 0.1% | 36% |
| 1 risk factor | 0.4% | 34% |
| 2 risk factors | 1.2% | 23.8% |
| 3 risk factors | 4.3% | 4.6% |
| 4 risk factors** | 5.6% | 0.3% |

** Only 1 bleed experienced in patients with all 4 independent risk factors

Risk factors were age 67 or older, warfarin, ear location, and flap or graft closure

**Discussion:**

There is an increased risk of bleeding in patients having skin cancer surgery in and around the ear. Our analysis was multivariate and demonstrated that all procedure types were associated with a greater bleed incidence on and near the ear.

Among ENT surgery cases, ear surgery has been regarded as low risk of requiring unexpected post operative admission due to complications.[202] Applying firm pressure dressings to defects closed on and around the ear often proved challenging.

We have previously identified three additional independent risk factors for bleeding complications following skin surgery by multivariate analysis[177]; age 67 or older, warfarin administration and closure with flap or graft. The risk of post operative bleeding is 1/1000 with no risk factors, 4/1000 with 1 risk factor and 12/1000 with 2 risk factors. Bleeding risk then escalates with 3 risk factors, (43/1000) and all 4 risk factors, (56/1000).

A blinded study has demonstrated that even experienced surgeons cannot predict whether

patients are on warfarin or aspirin at the time of operating. [203]

Surgeons should consider anticoagulant management and INR levels prior to operating. This study involves a single surgeon working in two surgical venues in one southern Australian regional city. The bleeding incidence reported may not reflect practice elsewhere.

**Conclusion:**

The only site where post operative bleeding risk was found to have increased risk followed excision on or immediately adjacent to the ear. An increased attention to haemostasis and dressings may be considered when surgery to the ear is planned. Curettage results in a similar bleeding risk to simple surgical excision and closure.

Bleeding following skin procedures is likely to be little more than an inconvenience and manageable with steps such as pressure, dressings and review. Occasionally (1:2000) the patient may come to wound exploration.

## *Summary*

Chapters 5 and 6 combine to provide substantial information on the risks of post operative bleeding following skin cancer surgery. In this chapter we found the ear and the skin adjacent to the ear were the only body sites where the clinician can predict an increased bleeding risk based on my data.
Chapters 1 and 2 addressed several infection questions. Chapters 3 and 4 addressed several questions regarding surgery below the knee. Now some post operative bleeding questions have been explored.

While we strive hard to minimize poor outcomes in skin lesion excision surgery, it is the patients who suffer as a result of these complications. It is the patients who must deal with the prolonged healing time, the pain, delays in returning to normal duties and the potential diminished aesthetic outcomes.

Chapter 7 takes a new direction. Rather than identifying skin surgery complications and their risk factors, we now look at the patient's perspective. Do patients feel less satisfied with their clinician if they suffer complications such as bleeding or infection? Or are there other aspects of the skin cancer surgery service that influence patient's perceptions to a greater extent?

# Chapter 7 Prospective study of long term patient perceptions of their skin cancer surgery

The studies thus far described in chapters 1 through 6 focus on complications of skin cancer surgery and their risk factors. But how do patients view experiencing such surgical complications?

These complications can result in increased pain, delayed healing, increased visits to the doctor, delays returning to normal duties, poorer aesthetic outcome and many other adverse impacts on our patients. But how do the patients view these complications?

The medical profession frequently associates lack of complications as a measurement of success of surgical interventions. [51] Regarding skin surgery, complications are frequently visible and readily apparent to the patient. It is not well known whether infection, bleeding, scar and wound complications affect the patient's perceptions of the skin surgical service. Does success from the clinician's view equate to success from the patient perspective? Or does the patient see other aspects of the service provided by the physician as more important to them.

Further, pain is another aspect of wound management we have not adequately addressed thus far. It has been considered that wounds that heal quickly generally involve less pain.[158]

We specifically sought feedback from my patients on the pain they experienced and their perceptions of our service through a prospective trial. We sought permission from patient's prior to their service including advice that we would be surveying them 6 to 9 months after their surgery to determine their views on complication, pain and the service provided.
This prospective trial has been published in the Journal of American Academy of Dermatology.[204] The complete manuscript of this trial is as follows:

# Prospective study of long term patient perceptions of their skin cancer surgery

**Abstract:**

Background: We identified factors that influence patient perceptions of their skin cancer surgery through a prospective study of patients referred to a single surgeon during 18 months**.**

Method: Patients having surgery resulting in a wound sutured and dressed were surveyed 6 to 9 months later. Monitoring for complaints continued for three years.

Results: In all, 74% of patients returned the survey (576 of 778). A total of 250 (43%) rated their scar excellent, 177 (31%) very good, 72 (12.5%) good, 40 fair (6.9%) and 14 (2.4%) poor or very poor. Age, sex, diagnosis, or closure method did not result in a variation in scar perception.

In all, 27.3% of scars (21 / 77) on the trunk were rated neutral or negative compared with 6.9% (33 / 476) of scars elsewhere, ($p<.001$) and 5% (15 / 305) of head and neck scars ($p<.001$). Complications did not change scar or overall evaluation ratings.

In all, 393 (68%) rated the overall service excellent, 145 (25%) very good, 22 (4%) good and 3 (0.5%) fair. No patient rated the service poor or very poor. Patients rating the service lower were most dissatisfied with scar appearance, time waiting before surgery, pain from the local anaesthetic, nursing care, follow up care, cost and written material.

In all, 99% of patients who rated their scar very good or excellent rated the overall service optimally, compared with only 85% of patients who rated their scar as good or worse.

**Limitations:** A single experienced surgeon in a southern Australia locale might not reflect the perceptions in other clinician's locations.

Conclusion: Complications and patient complaints do not identify patient dissatisfaction from cutaneous surgery. The patients' perception of their scars markedly influences their overall service perception. Patients experienced more dissatisfaction with repairs on the trunk.

## Introduction:

Patient perception of skin cancer surgery is poorly understood. We have previously described a 9.8% incidence of neutral or negative response to long term scar appearance[125]. Others have described a similar 13% neutral or negative wound assessment after excision of basal cell carcinoma.[205] Skin cancer is still predominantly managed by surgical excision and repair, and cosmetic outcomes from such procedures are usually well accepted, even in comparison to non operative procedures such as radiotherapy[205]. Using a randomized trial format the authors have previously demonstrated that the application of ointment to a wound does not change the overall patient assessment of cosmetic outcome.[125] Many other wound management methods have been adopted with the hope of improving scars but have shown no significant benefit in formal randomised control trials.[206, 207]

Wounds repaired under some tension are predominantly closed with sutures, with similar or somewhat improved results when compared with wounds closed with glues[208-212], staples[145, 213] or tapes[214-219].

Little is known of the aspects of skin cancer surgery that might result in a higher risk of the patient feeling neutral or negative toward their treatment experience or their scar. Patient perceptions of the outcomes of skin cancer management can differ from objective assessments[220]. It is not known how age, sex, diagnosis, type of procedure or complications affect patient satisfaction. It is possible that other aspects of skin cancer management might also alter patients' perception of service; waiting period before surgery, pain, dressing type, local anaesthetic, the operation, nursing care, procedure counselling, pathology counselling,[221] or even cost[222, 223].

Outcomes of wounds assessed over weeks rather than months are less likely to demonstrate a significant difference as wound healing progresses over several months. Study of wound healing perception should extend out at least three months to allow for scar remodeling[156].

## Methods:

Through a prospective longitudinal study, we sought to investigate whether patient demographics, diagnosis or treatment might influence a neutral or negative response to skin cancer surgery. This prospective study was conducted in accordance with the Declaration of Helsinki and was approved as part of a larger trial by the Barwon Health Research & Ethics Committee.

Inclusion criteria

Newly referred patients who attended a dedicated skin cancer surgery centre between July 1st 2002 and December 31st 2003 were offered enrolment in the prospective trial. Inclusion criteria required that the patient:

Be referred for management of skin lesion.

Have incisional or excisional surgery.

Have treatment resulting in a wound that was closed with sutures and to which a dressing was subsequently applied. Suturing was predominantly simple interrupted, with usage of vertical and horizontal mattress sutures at times where appropriate. Buried deep absorbable sutures were used sparingly before polyamide, particularly on larger defects or those with increased tension.

Exclusion criteria

Patients were excluded if the skin was contaminated or infected before surgery, the surgical site was not amenable to a moist occlusive dressing (eg. eyelid, lip), or the patient had a known allergy to the occlusive dressing.

Any patient who had more than one procedure during the trial period had the trial pertain to the first procedure only. Where patients had multiple tumours needing excision, the most concerning tumour was excised first.

One dermatologic surgeon (A.J.D) performed all procedures in one of two operating rooms. All surgery was undertaken using sterile surgical gloves, drapes and equipment. The surgeon wore a

surgically clean gown and a face mask. The site of all removed lesions were recorded and all specimens sent for histopathological examination. The dressings were moist and occlusive in nature[108, 109] and were applied by an experienced nurse who chose a dressing appropriate to site and patient considerations. Each patient was given a detailed postoperative instruction sheet, highlighting wound management and warning signs for complications. Patients who had a large excision and / or flap or graft were contacted by telephoned the day after surgery. Wounds were followed up clinically until wound healing was complete, at least until removal of sutures, and longer if there was skin flap or graft surgery involved or a complication was experienced.

Patients were counseled verbally and in writing, including a one page information sheet.

Complications record:

Any infected wounds were recorded and classified in the following predetermined groupings: purulent site, suture abscess, cellulitis, infective necrosis, large subcuticular abscess, regional lymphadenitis and septicemia. Wound infections were assessed clinically unless there was abscess formation or evidence of involvement beyond the local site. In these circumstances, a wound swab for culture was taken. In the absence of suppuration, a wound was considered infected if three of the following were present: discharge, pain, erythema, or induration. All wound infections were treated with oral Dicloxacillin (500mg four times daily) unless sensitivity or allergy deemed this to be inappropriate.

Complications were detailed and recorded. Adverse scar outcomes were classified as, wound spread, suture marking, hypertrophic scar, keloid, hyperpigmentation, hypopigmentation, wound depression, wound elevation, pronouncement of dog ears, and scar contracture.

Other adverse outcomes recorded included post operative bleeding, contact allergy to dressing, contact allergy to skin preparation, other contact dermatitis, recurrence of tumor, nodal or distant metastasis, dehiscence, pruritus, and persistent pain or nerve damage. Other adverse outcomes to be noted were; ectropion, nodal involvement, and distant metastases.

Questionnaire:

Six months after surgery, each patient was mailed a one-page survey to complete and return. (Figure 1) Patients not returning surveys were sent a repeated survey at 8 - 9 months after surgery. Patients who had multiple surgeries were asked to rate only their first procedure so as to minimize confusion.

All complaints either verbal or written, made by a patient about the doctor or the skin cancer surgery centre either direct or through a third party was documented for at least 36 months after each surgery.

## Statistical Analysis:

All key outcome incidences were analyzed using the chi-square test and the positive responders were compared with neutral or negative responders individually using 2 x 2 tables. The same process was used when examining other hypotheses. The only exception was our analysis of overall service

perceptions. There were no negative responders to this question so we compared very good and excellent (optimal) responses with good and fair (sub optimal) responses with, chi-square test with 2 X 2 tables.

**Results:**

A total of 926 patients were referred for surgery between July 1st 2002 and December 31st, 2003. A total of 148 patients were excluded from the study for the following reasons: wound sites were not amenable to a dressing (n=96), allergy to dressings (n=25), contaminated wounds at time of surgery (n=8), patient declined (n=13), age under 18 years (n=4) and patient unable to understand (n=2). The study group consisted of 778 patients with an average age was 59.3 ± 18 years.

These 778 patients had a total of 1801 surgical procedures during the 18 month study period.

In all, 69.4% of wounds were closed with elliptical excisions and direct closure. In all, 29.9% involved a random pattern skin flap and 0.7% required a skin graft.

Complications:

Post operative complications are detailed in Table 1. There were a total of 32 wound infections, (1.8%). Infections were predominantly local abscesses and cellulitis, and were treated with and responded to oral antibiotics, predominantly Dicloxacillin. There were no abscesses that needed draining; no infections required intravenous antibiotics, or hospitalization. No patient had more than one wound that became infected.

A sub-analysis of the excision region found a significant increase in the risk of wound infection in lower limb lesions. There were 225 lower limb lesions with an infection incidence of 4.4% compared with 1.4% for the remaining body areas ($p<.001$).

A sub-analysis of the first lesion versus second or subsequent lesions managed on each of the 778 patients revealed no significant difference in the incidence of skin infection, wound problems, bleeding and total complications between groups. (data not shown)

Survey at 6-months

A total of 576 patients returned the survey (74%). In all, 65.5% of men patients returned the survey (274 out of 418) compared with 83.9% of women (302 out of 360) ($p<.001$). Non-responders were not significantly different from responders with regard to age, sites of wounds or complication incidence.

Scar satisfaction:

Of the 576 respondents, 250 patients (43.4%) rated their scar as excellent, 177 (30.7%) rated their scar very good and 72 (12.5%) rated their scar as good. A further 40 patients (6.9%) rated their scar fair, 8 (1.4%) poor and 6 (1.0%) very poor. Sex and age did not correlate with the likelihood of rating a scar neutral or negatively, with responders in each age quartile demonstrating around a 10% neutral or negative scar assessment.

We analysed all the responses of patients who rated their wound neutral or negatively. (Table 2). Of note, scars to the trunk were more likely than scars

elsewhere to be rated as fair or worse. In all, 21 out of 77 trunk wounds (27.3%) were rated fair, poor or very poor compared with 33 out of 476 (6.9%) elsewhere on the body (p<.001). In all, 4.9% of patients (15 of 305) with surgery to the head and neck rated their scar fair or worse compared with 9.2% of lower limb scars (6/65) and 12.4% on the upper limb (12/97).

Analysis of face and head wounds was noteworthy for the high level of long term wound satisfaction. Of 305 head and neck wounds, 149 (48.9%) were rated excellent, 91 (29.8%) were rated very good, 41 (13.4%) good, 13 (4.3%) fair and 2 (0.7%) poor. No head and neck scar was rated very poor.

Patients were more likely to rate a scar neutral or negative if they were unhappy with the time taken to undertake surgery or that the pathology explanation was suboptimal. When a patient was unhappy with their scar they were more likely to be unhappy with the overall service. (Table 2).

Larger defects were more likely to be closed with a flap or a graft than direct closure. However, the choice or reconstruction did not affect patient satisfaction.

The presence or absence of complications in the post operative period did not correlate with a subsequent dissatisfaction. Patients with malignant and benign tumour surgery had equal rates of satisfaction. Patient's assessment of the duration before the first appointment with the doctor did not correlate with subsequent wound assessment. Details of the patient's assessment of the quality of practice explanations and timeliness of the service are in Table 3.

Wound pain:

Of the 576 respondents, 187 (32.5%) reported no post operative pain, 221 (38.4%) reported minimal pain that required no analgesia, 135 (23.4%) reported pain that was controlled with paracetamol, 16 (2.8%) required analgesia stronger than paracetamol and 4 patients (0.7%) described severe pain that did not respond to combined oral analgesics.

Dressing feedback:

In all, 284 of the 576 respondents (49.3%) found the dressing to be no inconvenience to them. 259 (45%) rated the dressing as a nuisance while only 12 patients (2.1%) found the dressing to be disruptive or intolerable.

Overall assessment:

When asked for their overall assessment of the service 6 to 9 months after surgery, 393 of the 576 (68.2%) rated the service excellent, 145 (25.2%) very good, 22 (3.8%) good, and 3 (0.5%) fair. No respondent described the overall service as poor or very poor.

We sought to further analyse aspects that resulted in the 25 patients rating the service good or fair (suboptimal) rather than very good or excellent, (optimal).

Answers to questions from the 25 respondents who rated service as suboptimal were compared with those rating the service optimally. (Table 4).The following characteristics correlated with a suboptimal rating: male sex, perceived undue time taken between consultation and surgery, assessment of the local anaesthetic, rating of the actual

operation, nursing care assessment, follow up care rating, cost of service rating, rating of written material provided and self scar assessment.

There were four aspects of service that were consistently and repeatedly highlighted by those rating the overall service as suboptimal. These were scar assessment, cost of service, follow up care, and written material provided. In each of these 4 parameters, over two thirds of respondents providing a suboptimal rating came from the 25 patients who rated the overall service as suboptimal. In contrast, less than one third of respondents providing a suboptimal rating for these parameters came from the 538 patients that considered the overall service optimally. In each case the difference was highly significant.

No patient rated the overall service as suboptimal unless at least two of these four aspects were rated sub optimally. Four patients nominating the service as good indicated two areas in which their assessment was suboptimal. Five patients highlighted 3 of these 4 parameters as suboptimal, thirteen listed all 4 parameters. The three patients who rated the overall service as fair indicated all 4 parameters were suboptimal.

Complaints:

Aside from the surveys, no complaints were made by any patient during the trial period up or until December 31st 2006. There was no verbal or written complaint to the doctor or the staff. Further, no complaints were made to any third parties about us and then forwarded or reported to us. The survey invited respondents to add comments after the specific questions. (Figure 1) No patient chose to make a complaint within the "comments" section.

**Discussion:**

Just more than 90% of patients in this study rated their long term scars as excellent, very good or good. This is consistent with previous smaller studies.[205] These data showed that more than 99% of patients who rated their scar very good or excellent also rated the overall service very good or excellent. In contrast, only 85% of patients who rated their scar good, fair, or worse rated the overall service very good or excellent. It is clear that end points for quality can be very different from end points of service as assessed by the patients. Although surgeons are conscious of complications such as tumour recurrence and strive to minimise such adverse outcomes, patients did not associate complications with suboptimal scars or poor quality of service.

This study demonstrated that patients were more likely to consider the scar suboptimal when it was on the trunk, including the chest, back and abdomen. In contrast, patients were overwhelmingly very satisfied with surgical scars to the face and head.

In response to these findings, we have developed a fact sheet explaining the characteristics of scars to the trunk, including the higher and problematic incidence of hypertrophic scars, wound spread and keloid formation.

Surgeons excising lesions from the trunk may consider using reconstructive techniques that reduce the incidence of widened scars, hypertrophic scars

and keloids. These include the modified buried vertical mattress suture[79]and the incorporation of both deep subcuticular and epidermal sutures. Such deeper sutures have been demonstrated to result in better patient scar acceptance when used after abdominal[224], hip[225, 226] and leg surgery[145]. Other studies, however, have not found such an advantage.[129, 213]

The infection incidence and distribution of infection in this study is consistent with previously published data in a larger study.[122] Patients scheduled for excisions below the knee can be advised that they are subject to higher rates of infection and that more prolonged and involved post operative care can be expected.

Other than location on the body, this study demonstrated that patients were more likely to rate a scar poorly with a perceived delay before surgery or if they were not fully satisfied with the explanation of the pathology results. Patients expressed dissatisfaction with delays as short as several days between learning that a skin lesion needed excision and the eventual surgery.

There were several instances when the patient scar assessment did not correlate with our assessment. For example, there were two patients seen over six months after surgery who rated their scar as poor despite the fact that the study investigators had to check photographic records to identify the site of surgery as no visible scar was apparent. Similarly, there were patients who rated their scar excellent when the surgeon would have preferred a more aesthetic result. A more formal analysis of patient versus clinician assessment of scar was not possible as relatively few patients were examined 6 to 9 months after their procedure.

Two thirds of the patients did not require analgesia after excision of skin lesion. Those who required analgesia predominantly controlled their pain with paracetamol. Wound dressings were well tolerated by patients with few regarding dressing as more than just a minor nuisance.

The study has many limitations other than reliance on patient scar assessment in the absence of an independent evaluator. The study involved only a single experienced skin cancer surgeon in a southern Australian temperate climate. Wound infections can be substantially higher in more tropical regions, including northern Australia.[227] The study surgeon may be more experienced and skilled at facial surgery than trunk surgery, possibly accounting for the large discrepancy in wound satisfaction between trunk scars and other scars. Women were more likely to return the survey than men. It is unclear whether this had any effect on the validity of the study.

Five patients who had no out of pocket expense for their skin cancer management rated the cost of the service as “fair”. These were pensioners who assigned the total cost of their treatment to the public health system (Medicare Australia). They may have chosen to describe the cost as “fair” in the belief that a fair cost for pensioners is that Medicare Australia should meet the entire account. As such, the wording of our cost question may have been inadequate.

## Conclusion:

To maximise patient satisfaction with respect to surgical skin cancer services, the surgeon needs to consider aspects of service beyond minimising tumour recurrence, minimising complications and addressing complaints if and when they are made.

The most important factor influencing a patient's overall assessment of a skin cancer service is their perception of the final aesthetic outcome of the wound.

Table 1: Complications experienced

| | Total |
|---|---|
| Number of patients | 778 |
| Number of operations | 1801 |
| Average age of patients, y | 59.3 ± 18 |
| Male | 418 (53.7%). |
| Average operations per patient | 2.3 |
| Wound infection | 32 (1.8%) |
| Suture abscess | 11 |
| Cellulitis | 17 |
| Infective necrosis | 2 |
| Purulent sutured wound | 2 |
| Lower limb excisions (n=225)) | 10 |
| Scar complications - other | 12 (0.7%) |
| Skin necrosis | 7 |
| Hypertrophic scar | 3 |
| Wound elevation | 1 |
| Wound depression | 1 |
| Post operative bleed | 12 (0.7%) |
| Wound dehiscence | 13 (0.7%) |
| Other complications | 10 (0.6%) |
| Total complications | 79 (4.4%) |

Table 2: Comparison of patients who perceived scar positively versus neutral or negative patient self assessment

| Parameter | | Total no. responding | Rating wound positive, No. | % rating wound positive | Rating wound neutral or negative | Rating Wound neutral or negative,% | No. not rating wound | P value |
|---|---|---|---|---|---|---|---|---|
| Sex | Male | 261 | 232 | 88.9 | 29 | 11.1 | 5 | NS |
| | Female | 292 | 267 | 91.4 | 25 | 8.6 | 8 | |
| Age, y | 58 or older | 300 | 271 | 90.3 | 29 | 9.7 | 6 | NS |
| | Under 58 | 253 | 228 | 90.1 | 25 | 9.9 | 7 | |
| Past skin cancers | Yes | 73 | 66 | 90.4 | 7 | 9.6 | 3 | NS |
| | No | 480 | 433 | 90.2 | 47 | 9.8 | 10 | |
| Skin site | Trunk | 77 | 56 | 72.7 | 21 | 27.3 | 0 | P<.001 |
| | Limbs or head & neck | 476 | 443 | 93.1 | 33 | 6.9 | 13 | |
| Benign or malignant | Benign | 272 | 245 | 90.1 | 27 | 9.9 | 7 | NS |
| | Malignant | 281 | 254 | 90.4 | 27 | 9.6 | 6 | |
| Analgesia | Required analgesia | 149 | 131 | 87.9 | 18 | 12.1 | 5 | NS .27 |
| | No analgesia | 402 | 366 | 91.0 | 36 | 9.0 | 0 | |
| Complications | Yes | 33 | 28 | 84.8 | 5 | 15.2 | 0 | NS 0.28 |
| | No | 520 | 471 | 90.2 | 49 | 9.8 | 13 | |
| Operation | Direct closure | 400 | 362 | 90.5 | 38 | 9.5 | 9 | NS |
| | Other | 153 | 137 | 89.5 | 16 | 10.5 | 4 | |
| Dressing experience | No issue | 276 | 249 | 90.2 | 27 | 9.8 | 0 | NS |
| | Nuisance or negative | 275 | 250 | 90.9 | 25 | 9.1 | 5 | |
| Assessment of time to appointment | VG or excellent | 514 | 463 | 90.1 | 50 | 9.9 | 2 | NS |
| | Good or fair | 36 | 32 | 88.9 | 4 | 11.1 | 3 | |
| Assessment of time to surgery | VG or excellent | 515 | 477 | 93.8 | 38 | 6.2 | 5 | P<.001 |
| | Good or fair | 33 | 17 | 51.5 | 16 | 48.5 | 0 | |
| Rating of surgery explanation | VG or excellent | 507 | 457 | 90.1 | 50 | 9.9 | 5 | NS |
| | Good or fair | 40 | 36 | 90.0 | 4 | 10.0 | 0 | |
| Rating of pathology explanation | VG or excellent | 497 | 454 | 91.3 | 43 | 8.7 | 5 | .003 |
| | Good or fair | 50 | 39 | 78.0 | 11 | 22.0 | 0 | |
| Overall assessment | VG or excellent | 498 | 455 | 91.4 | 43 | 8.6 | 0 | .006 |
| | Good or fair | 54 | 43 | 79.6 | 11 | 20.4 | 0 | |

NS, Not significant.

Table 3: Patient assessment of the timeliness and quality of explanation of services

| | Excellent | Very good | Good | Fair | Poor | Very poor | Did not answer |
|---|---|---|---|---|---|---|---|
| Time until first appointment with doctor | 359 (62.3%) | 167 (29.0%) | 34 (5.9%) | 3 (0.5%) | 0 | 0 | 13 |
| Time until operation was undertaken by doctor | 323 (56.1%) | 204 (35.4%) | 33 (5.7%) | 3 (0.5%) | 0 | 0 | 13 |
| Procedure explained | 265 (46.0%) | 254 (44.1%) | 35 (6.1%) | 9 (1.6%) | 0 | 0 | 13 |
| Pathology explained | 275 (47.7%) | 238 (41.3%) | 41 (7.1%) | 6 (1.0%) | 3 (0.5%) | 0 | 13 |
| Written explanations provided | 280 (48.6%) | 239 (41.5%) | 40 (6.9%) | 9 (1.6%) | 4 (0.7%) | 1 (0.02%) | 13 |

Table 4: Comparison of patients who rated overall service very good or excellent (optimal) versus those who rated the service as suboptimal

| Parameter | | Total no. responding | Rating service optimal ,No. | Rating wound optimal, % | Rating service suboptimal, No. | Rating wound suboptimal, % | P value |
|---|---|---|---|---|---|---|---|
| Sex | Male | 266 | 249 | 93.6 | 17 | 6.4 | .033 |
| | Female | 297 | 289 | 97.3 | 8 | 2.7 | |
| Age | 58 or older | 304 | 289 | 95.1 | 15 | 4.9 | NS .54 |
| | Under 58 | 259 | 249 | 96.1 | 10 | 3.9 | |
| Past skin cancers | Yes | 75 | 71 | 94.7 | 4 | 5.3 | NS .68 |
| | No | 489 | 468 | 95.7 | 21 | 4.3 | |
| Skin site | Trunk | 84 | 79 | 94.0 | 5 | 6.0 | NS .46 |
| | Limbs or head & neck | 479 | 459 | 95.8 | 20 | 4.2 | |
| Benign or malignant | Benign | 274 | 264 | 96.4 | 10 | 3.6 | NS .37 |
| | Malignant | 289 | 274 | 94.8 | 15 | 5.2 | |
| Analgesia | Required analgesia | 155 | 148 | 95.5 | 7 | 4.5 | NS .96 |
| | No analgesia | 408 | 390 | 95.6 | 18 | 4.4 | |
| Complications | Yes | 34 | 31 | 91.2 | 3 | 8.8 | NS .2 |
| | No | 529 | 507 | 95.8 | 22 | 4.2 | |
| Operation | Direct closure | 405 | 390 | 96.3 | 15 | 3.7 | NS .72 |
| | Other | 159 | 149 | 93.7 | 10 | 6.3 | |
| Dressing experience | No issue | 280 | 271 | 96.8 | 9 | 3.2 | NS .16 |
| | Nuisance or negative | 283 | 267 | 94.3 | 16 | 5.7 | |
| Assessment time to appointment | V G or excellent | 524 | 502 | 95.8 | 22 | 4.2 | NS .21 |
| | Good or fair * | 34 | 31 | 91.2 | 3 | 8.8 | |
| Assessment | V G or excellent | 521 | 501 | 96.2 | 20 | 3.8 | .004 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Good or fair * | 35 | 30 | 85.7 | 5 | 14.3 | |
| Surgery explanation | V G or excellent | 518 | 497 | 95.9 | 21 | 4.1 | .08 |
| | Good or fair * | 40 | 36 | 90.0 | 4 | 10.0 | |
| Pathology explanation | V G or excellent | 508 | 485 | 95.5 | 23 | 4.5 | NS |
| | Good or fair * | 50 | 48 | 96.0 | 2 | 4.0 | |
| Rating of local anaesthetic | V G or excellent | 500 | 484 | 96.8 | 16 | 3.2 | .001 |
| | Good or lower | 61 | 52 | 85.2 | 9 | 14.8 | |
| Rate the operation | V G or excellent | 511 | 502 | 98.2 | 9 | 1.8 | .001 |
| | Good or lower | 49 | 33 | 67.3 | 16 | 32.7 | |
| Nursing care assessment | V G or excellent | 545 | 532 | 97.6 | 13 | 2.4 | .001 |
| | Good or fair * | 18 | 6 | 33.3 | 12 | 66.7 | |
| Follow up care rating | V G or excellent | 507 | 502 | 99.0 | 5 | 1.0 | .001 |
| | Good or lower | 51 | 31 | 60.8 | 20 | 39.2 | |
| Cost rating | V G or excellent | 427 | 422 | 98.8 | 5 | 1.2 | .001 |
| | Good or lower | 135 | 115 | 85.2 | 20 | 14.8 | |
| Written material rating | V G or excellent | 486 | 478 | 98.4 | 8 | 1.6 | .001 |
| | Good or fair ** | 72 | 55 | 76.4 | 17 | 23.6 | |
| Scar assessment | V G or excellent | 426 | 422 | 99.1 | 4 | 0.9 | .001 |
| | Good or lower | 138 | 117 | 84.8 | 21 | 15.2 | |

NS, Not significant

* There were no patients rating this category or overall service as poor or very poor.

Figure 1 Survey of participants 6 to 9 months following lesion excision.

How would you rate the wound discomfort from the time of the surgery?
No pain
Minimal discomfort that did not require pain killers
Mild pain, relieved by Panadol, Panamax or Herron Paracetamol
Moderate pain that required stronger pain killers to gain relief
Bad pain that could not be relieved with pain killers
The worst pain I have ever experienced

How would you rate the inconvenience of the dressing from the time of the surgery?
No inconvenience
A nuisance, but did not interfere with things
Very disruptive or embarrassing to me
Could not tolerate the dressing

Rate our performance as either:
Excellent, Very Good, Good, Fair, Poor or Very Poor to the following 12 questions:

How would you rate the time taken from being referred to Skincanceronly Clinic until the time you were assessed by our Doctor?
How well was the procedure explained to you in advance?
How would you rate the time taken to have your skin surgery?
How effective was the local anaesthetic?
How would you rate the actual operation?
How would you rate the nursing / reception staff?
How well was the pathology result explained to you?
How good was the follow up care by Skincanceronly Clinic?
How good was the final look of the scar?
How would you rate the cost of your treatment at Skincanceronly Clinic?
How good was any written material provided?
Overall, how do you rate our service?

Please feel free to add any comments:

## *Summary:*

While chapters 1 through 6 expanded our knowledge base of skin surgical complications, they did not provide information on the patient's view regarding suffering such complications. We now have further information regarding how patients view their skin cancer surgery. The patient's viewpoint differs from that of the clinician. Suffering complications did not result in an increased likelihood of patient dissatisfaction.

26% of the patients did not return the survey. These patients may have been more dissatisfied that those who responded. Also, patients who had more than one lesion excised may have had difficulty recalling which lesion was excised first in their reflections on the skin service.

# Chapter 8 Other publications

Chapters 1 through 7 describe the original studies that comprise the core works of this thesis. Other manuscripts have been published designed to assist doctors in better understanding management of skin cancer including managing complications of skin surgery.[228-236] They do not include original research.

Australian Family Physician published 13 peer reviewed and published manuscripts for which the author was Dr. Anthony Dixon.
These included the "23 Golden Rules of Managing Skin Cancer"[229] as well as 12 pieces geared at providing a broad update on managing skin cancer for the general practitioner audience.[228, 230-243] These manuscripts are reproduced in full in the Appendix to this thesis.

Two other manuscripts have been published providing a short literature review on two separate controversies in cutaneous oncology. One manuscript reviewed the role of sentinel node biopsy in managing melanoma. The second discussed the possible role or arc welding as an ultraviolet source that might lead to skin cancer production.

The role of sentinel node biopsy in managing melanoma was published in "CML Dermatology" in 2006.[244] The full text of this manuscript follows:

## *MSLT spells a halt to sentinel lymph node biopsy*

Background

In 1892 Dr. Herbert Snow observed that melanoma patients who developed lymph node involvement invariably died of their malignant melanoma. Ever since that time, clinicians and researchers have been trying to find a way to turn this observation into a better outcome for our patients. Snow proposed that all melanoma patients have their regional lymph nodes resected[245]. However, several subsequent random control trials have failed to demonstrate a survival advantage from elective lymph node dissection (ELND).

80% of the nodes resected through ELND had no melanoma involvement. Patients were being subjected to considerable morbidity for no apparent benefit. ELND has long been abandoned from routine management of malignant melanoma. But if we knew which 20% of patients had the melanoma in their nodes, maybe these melanoma patients could be selected for lymph node dissection.

Sentinel node biopsy described:

100 years later, Dr. Donald Morton described sentinel lymph node biopsy (SNB); a method of identifying patients that have early node

involvement such that these patients could then be offered completion lymphadenectomy (CL)[246]. Morton's approach promised three advantages for patients: improved survival, enhanced patient information and guidance for future management.

SNB involves the use of lymphoscintography and / or dye to identify the sentinel node (SN). The identifier is injected around the site of the primary melanoma, enabling the material to be carried through the lymph system to the SN. Dissection of the node basin can then identify this SN and it is removed leaving adjacent nodes in place. Involvement of melanoma in the processed SN would then direct management to CL.

Lens[247] identified that the likelihood of melanoma involvement in SNs is proportional to the Breslow thickness of the primary tumor. 1% of tumors below Breslow 0.75mm will have SN involvement. 8.3% of patients with Breslow 0.75 to 1.5 mm melanomata will have positive SNs, 22.7% of patients with Breslow 1.5 to 4 mm and 35.5% of more advanced tumors.

The original idea of SNB involved resection of the SN at the time of resection of the primary tumor. In two separate studies, Leong[248] and Evans[249] have identified that outcomes are not different if the primary tumor excision is undertaken before the SNB. Given the only management of melanoma that improves outcome is prompt wide local excision (WLE), a lengthy delay for tumor resection just to enable simultaneous SNB is not justified.

Multicenter trial of SNB

After developing the concept of SNB, Morton went on to test the efficacy of this technique through a well designed and powered random control trial known as the Multicenter Selective Lymphadenectomy Trial (MSLT – 1). This trial was based at the John Wayne Cancer Institute in Santa Monica California. The multinational centers involved in the trial included Sydney Australia where a large number of patients were recruited for the trial.

MSLT excluded melanomata with Breslow below 1 mm. This has proved an appropriate exclusion given the low incidence of positive SNs in patients with early tumors.

In this study, 1200 patients were randomized to SNB with all those having positive nodes proceeding to CL. There were 800 controls who did not have SNB performed, but had lymphadenectomy if and when nodes became subsequently involved. The survival data from the MSLT – trial has now been presented at the American Society of Clinical Oncology meeting in May 2005. This same data has also been presented to the 6$^{th}$ World Congress on Melanoma in September 2005 and American Society for Dermatologic Surgery Annual Meeting in October 2005.

The five year survival for patients in the SNB group was 87%, versus 86% in the control group (p=0.4). The sentinel node patients gained no survival benefit.

Sub-analysis:

Unfortunately a flawed sub-analysis of this study has created more interest than the core data. Morton showed that SNB positive patients demonstrated a 22% 5 year survival advantage over patients who later developed tumor involved nodes. Such a so-called advantage is hardly surprising. This simply reminds us those patients likely to develop involved lymph nodes fare better than patients who have proven lymph node involvement.

At the end of the day, the one comparison that is valid in the MSLT study is the primary outcome for which the study was designed, the 5 year survival of treatment versus control arms. Their outcomes are the same.

An earlier study by Kretschmer[250] has suggested an outcome benefit for SNB patients. This paper is much quoted but flawed. The study compared SNB patients with those who later developed positive clinical nodes and had delayed lymph node dissection (DLND). 5 year survival for DLND patients was 50.2% compared with 62.5% for SNB positive patients.

However, the study did not involve patients who did not have SNB and did not develop clinical nodes. As such, the study simply compared those who might develop metastatic nodal involvement with those that did develop involved nodes. The discussion within this manuscript goes to some length to explain how lead time bias was factored into the analysis. Lead time bias was not the predominant flaw in the analysis, rather it was the failure to compare patients on an "intention to treat" basis.

How much melanoma in the SN?:

In the MSLT trial, any melanoma in the SN meant it was deemed positive and CL was offered. But there is increasing evidence that small amounts of melanoma within the SN may not be of great concern. Vuylesteke[251] demonstrated that patients with Breslow thickness less than 2.5 mm who had positive SNs with tumor load of less than 0.3 mm did not have additional nodes involved with melanoma. They had excellent survival prospects and did not need to have CL.

The significance of a small amount of melanoma involvement in a node (or micrometastasis) was further questioned by Giblin et al[252]. If there are tiny foci of melanoma in SNs then it is difficult to justify further offering the patient CL. At times there will be pockets of melanoma in peripheral sinuses of SNs which, apparently for immunological reasons, do not progress to metastasis. It would be devastating to effect a block dissection and cause morbidity such as lymphoedema only to find predictably uninvolved nodes in the large dissection specimen.

Starz[253] data demonstrates any SN involvement of less than 1 mm has no adverse prognostic significance. Spanknebel[254] demonstrated that micrometastases identified only on immunochemical staining have no adverse prognostic significance.

We can no longer justifiably advise all our SN positive patients to proceed to CL. Cochran[255] has demonstrated that only one third of patients with positive SNs will have melanoma in adjacent nodes. Indeed proceeding to CL may only be appropriate if the original tumor had a large Breslow thickness, there was considerable volume of melanoma in the SN and also dense dendritic cells in the SN. It is difficult to justify advising a patient with an early Breslow tumor to have the SNB procedure if we would not then advise proceeding to CL even when the SN contained melanoma.

Complications of SNB:

The MSLT trial demonstrated that 10.1% of patients who undergo SNB, develop complications.[256] Indeed the complication rate rose to 37.2% in those patients who were SNB positive and went on to CL. SNB complications are such a problem on the head and neck that some centers exclude patients who have primary head and neck tumors. For example, some 25% of these SNs are located within the parotid gland, with dissection to identify and remove the node risking facial nerve damage.[257]

If SNB provides no survival benefit but is associated with such concerning morbidity figures, there must be some other reason to justify patients undergoing this procedure.

Information for patients:

Mohrle et al[258] studied 283 SLN patients finding that these patients gained no benefit in survival time. While these findings supported the MSLT data, this paper also raised again the value of SNB as a means of providing accurate advice for our patients.

Zogakis[47] demonstrated that 9% of SNB negative patients developed tumor recurrence. Similarly, Gershenwald[259] demonstrated 13% of patients who were SNB negative would develop recurrence somewhere else within three years. Clearly SNB negative patients are surviving poorly compared with patients who did not have SNB and did not subsequently develop nodal involvement.

SNB negative patients can be advised that they are less likely to develop later metastatic disease. But they cannot be advised that metastatic disease has been ruled out. The advice that one's SN is negative simply means a slightly lower risk, not a removed risk of mortality from the malignancy. Melanoma can spread via the circulatory system. Melanoma patients need careful follow up even if they have a negative SNB.

Melanomata with large Breslow thickness are associated with increased risk of mortality and increased risk of SN positivity. As such, to what extent is that added risk that comes with having a SN positive merely reflect the underlying Breslow thickness?

Roka[260] undertook a multivariate analysis of risk factors for survival in malignant melanoma. The analysis was able to separate the predictive value of Breslow thickness from the predictive value of SNB status. Roka found that SNB was not predictive of overall survival. Rather, Breslow thickness was the

only independent predictor of overall survival. In an analysis of disease free survival, Breslow thickness, SNB status and ulceration were all predictive. Breslow thickness remains the single most important detail of a melanoma when it comes to providing information and advice to our patients.

In transit melanoma:

Thomas et al[101] raised the concern that the SNB procedure may increase our patient's risk of subsequent in transit and loco-regional metastases. These same investigators published the excellent random control trial of 1 cm versus 3 cm clearance for high risk melanoma in the New England Journal of Medicine[261]. In this metanalysis[101], they demonstrated an incidence of in-transit metastasis in SN positive patients following CL was 4 – 5 times that expected for that mean Breslow thickness. In other words, it is doing synchronous or near-synchronous wide excision and completion lymphadenectomy, while melanoma cells are still in transit, which may cause the increased incidence of in-transit disease.

Others have not confirmed this in transit risk[262]. Van Poll [263] demonstrated Sydney patients were not more likely to develop in transit disease following SNB. Kretschmer [264] refuted Thomas concluding that SNB and CL avoid later tumor recurrence and prolong disease free survival in melanoma patients. Unfortunately this study has the same "intention to treat" problems that were characteristic of their earlier work[250].

Regardless of whether or not SNB leads to an increased risk of in transit and loco-regional disease or not, the vital impact for our patients is whether they will live longer through the SNB procedure. The MSLT study demonstrates they will not. As a sufficient number of authors, independently, have now described an increased incidence of in-transit metastasis, all patients considering this operation should be warned of this possible risk.

Does SNB guide future management?:

We do not have treatments for metastatic melanoma that prolong life. Chemotherapy, radiotherapy and other approaches have not demonstrated improved long term survival for our melanoma patients. We cannot even justify CL in SNB positive patients with tumor load in the SN beneath 1 mm.

This situation might change in the future. Emerging treatments such as B RAF inhibitors[265] may provide a future management for patients with early nodal disease. If such treatments are demonstrated to improve patient survival, then we may have a reason to identify early metastatic disease through the SNB procedure.

Abandon SNB?:

Medalie and Ackerman[266] consider that SNB now lacks any value to the extent that it should be abandoned. Thomas[101] does not suggest the technique be abandoned, but does consider the technique should no longer be used outside of randomized control trials (RCTs). Indeed given the lack of benefit of SNB and the significant morbidity that comes with the procedure, it is now difficult to

justify the test outside of RCTs. At best SNB provides ***some*** extra advice for patients with melanomata between Breslow 1 and 3 mm in thickness.

Conclusion:

SNB promised three things; improved survival, enhanced patient information and guidance for future management. SNB does provide added information for patients who have tumors with Breslow thickness between 1 and 3 mm. In all other respects the SNB procedure has not delivered on its promise.

SNB may have a role in the future if and when an adjuvant melanoma therapy is developed that improves survival in patients with demonstrated early metastatic involvement.

The MSLT results are very helpful. If a pharmaceutical product performed as poorly as SNB as shown in MSLT the product would never achieve FDA approval, but rather it would be abandoned or invited to proceed to phase iii trials. Why should a surgical management be regarded any differently?

It is now difficult to justify ongoing usage of the SNB procedure other than in the context of an RCT to evaluate possible future medical or surgical interventions for melanoma patients. SNB is certainly not a "standard of care" for melanoma patients.

Another original manuscript shedding light on non solar causes of skin cancer was published in the Medical journal of Australia in 2004.[267] Specifically, we discussed the possible role of ultraviolet from arc welding being a contributing cause in skin cancer development. The full manuscript published is as follows:

## *Ultraviolet radiation from welding and possible risk of skin and ocular malignancy*

Introduction:

The overwhelming majority of skin cancers are caused by exposure to ultraviolet radiation (UVR) from the sun. However, there are non-solar sources of UVR that may also cause cancer. The purpose of this review is to explore the evidence that radiation from the welding arc may also be a significant risk to welding trades people, people near arc welding trades people and to occasional users of arc welding processes such as mechanics, sculptors and farmers.

A literature search was conducted using Pubmed and Synergy. The key words used in the search were: "basal cell carcinoma", "squamous cell carcinoma", "skin cancer", "melanoma", "weld", "welding" "arc", "radiation" and "ultraviolet".

Ultraviolet Radiation and Cancer:

The full spectrum of UVR can be classified into three groups based on wavelength. Ultraviolet "A" (UVA) spans UVR with the longest wavelength (400 – 315 nm). Over 98% of solar UVR exposure is UVA. UVA penetrates the skin more deeply than Ultraviolet "B" (UVB) or Ultraviolet "C" (UVC), but is less associated with DNA damage and the formation of pyrimidine dimmers. [268] [269]

UVB includes UVR with shorter wavelengths (315 – 280 nm). UVB accounts for less than 2% of our solar UVR exposure because much of it is absorbed in the upper atmosphere. UVB accounts for most of the DNA damage within skin cells and most of the resultant skin cancers. [268] [269]

UVC covers the range of UVR with the shortest wavelength (280 – 100 nm). UVC exposure is insignificant for most people because solar UVC is readily absorbed in the atmosphere before the damaging radiation reaches the earth's surface. Knowledge of the effects of UVC on skin is less clear. However, UVC may be as dangerous to skin as UVB. [269] [270]

Arc welding produces the full spectrum of UVR. The short distance between the arc and the welder's skin may not be sufficient to absorb most of the UVB and UVC. Arc welders may be at significantly increased risk of developing actinic skin damage including malignant melanoma and non-melanoma skin cancer (NMSC), particularly if they have inadequate protection.

Apart from producing UVR, arc welding can also produce thermal burns on the skin of welders. Such burns may also contribute to skin developing skin cancer.[271]

Review of evidence

Table 2 summarizes the limited studies into the risk of skin cancer from arc welding. The only formal case control study was by Emmett and co-workers [272], who studied 77 welders, 75 other workers exposed to welding and 58 non-exposed workers. Emmett did not find a link between welding and the development of cancer on the skin of welders.

A number of features of the Emmett study are noteworthy. They studied one workplace, described by Emmett as "a plant where both management and workers were careful to maintain hygienic practices. . . well-run welding operations which use and enforce current safety standards. . .' He also said that; '… it is not believed these results can be extrapolated to welding operations which do not employ good practices."

The study looked at relatively young people. The average age of the workers examined was 45. The average age of welders was 43 and they had been working for the same employer for an average of 16.9 years. Skin cancer often occurs decades after the significant UVR exposure. It is conceivable that the UVR skin damage experienced by those workers had not manifested as actinic changes because they were relatively young.

The Emmett study involved workers welding predominantly with mild steel. Higher intensity welding such as welding aluminium was not explored. Formal medical histories of those examined were not available.

Furthermore, the Emmett study did not include examination for naevi. At the time the relationship between atypical naevi and malignant melanoma was not understood. We now recognize that multiple atypical naevi are associated with a

significant increase in the subsequent incidence of malignant melanoma.[273]

The evidence linking ocular melanoma with welding is contradictory (Table 2). In an overview on the topic, Tenkate [274, 275] postulated that UVR from arc welding was one of the most intense artificial sources of optical radiation.

Effect of Welding Technique on UVR Exposure:

Lyon [276] describes common welding techniques and variables and the relative radiation exposure from each. These variables and their impact on UVR are summarized in Table 3.

UVR is associated with arc welding processes which include manual metal arc, gas metal arc (GMA) and gas tungsten arc welding. GMA welding generally produces the most radiation of the common welding processes and aluminium is generally welded by GMA welding. (Table 4)

It should be noted that not all welding processes involve striking an arc. These forms of welding produce minimal UVR. Welding processes and their UVR emissions are summarized in Table 5.

Skin protection is essential to minimize UVR exposure. Suitable protection while arc welding includes wearing suitable gloves as well clothing over the arms and forearms down to the gloves. For welding trades-people working in an uncomfortable environment, operator comfort and convenience are a major factor. In particular, the radiant heat from welding can be quite uncomfortable and welding on a hot day compounds the problem. The temptation is to discard heavy welders' clothing in favour of light, summer clothing. The wearing of short sleeved shirts and / or no gloves while welding places the skin of the forearm and hand at considerable UVR exposure. Many welders recognize the red triangle that develops over the manubrium. This erythema commonly results from the welder forgetting to fasten the top shirt buttons before welding.

Aside from full time welders, there are many trades-people who perform welding as a small part of their occupation (eg; motor mechanics) and these people often find it inconvenient to put on protective clothing in order to undertake a quick job.

A third group of welding workers, sculptors and trades-people doing highly intricate work, also experience difficulties in achieving fine details with heavy clothing over their forearms and thick gloves on their hands.

Furthermore, while trades-people are invariably educated in health and safety issues when learning to weld, other workers in the same workplace may not be. It is common to see welders working in a factory with thick clothing and a suitable mask while other people in the vicinity have little or no skin protection. Sometimes these are assistants supporting the metal being fused. Exposure to UVR of all people working in the area of a welding arc should be considered.

Recommendations:

While there remain many unanswered questions regarding arc welding and skin cancer risk, there are some principles that we can consider in prevention of skin cancer. These include:

When skin cancer patients deny a significant history of sun exposure, arc welding should be considered a possible cause.

Welders can be advised regarding appropriate clothing and be encouraged to choose sunscreens that include UVC protection. Workers welding aluminium risk the highest exposures to artificial UV and can be so advised.

The lack of quality studies means there is uncertainty about the risk of skin cancers from arc welding operations and further investigations are needed.

Issues that should be considered in any future study include:

- Examining workers who commenced welding at least 25 years prior to the study.
- Workers using varying arc welding processes, shielding gases and metals.
- Part time welders who do not adequately protect themselves.
- Examining for atypical naevi as well as actinic keratoses, NMSC and malignant melanoma.
- Obtaining histology on any suspicious lesions.
- Background actinic damage from solar UVR.
- Similarly, other risk factors such as skin type need consideration.

Table 1: Evidence linking development of cutaneous malignancy with arc welding

| Investigator | Finding | Level of evidence |
|---|---|---|
| Emmett et al [272] | Case control study of 77 welders and 133 other workers in the same factory. Welders more frequently suffered erythema and cutaneous burns. Neither welders nor controls were found to have NMSC. The only melanoma identified was in a non welder. Only seven workers demonstrated actinic keratoses. | Level III.2 |
| Currie & Monk [277] | Review five cases of NMSC in welders – advise that this non solar source of UVR should not be overlooked | Level IV |

Table 2: Evidence linking development of ocular malignancy with arc welding

| Investigator | Findings | Level of evidence |
|---|---|---|
| Holly et al [278] | Case control study of 221 patients with uveal melanoma. Welding exposure increases the risk of developing intraocular melanoma | Level III.2 |
| Guenel [279] | Case control study of 50 patients with uveal melanoma. Identified increased risk through welding and considered ultraviolet the likely cause | Level III.2 |
| Pane [280] | Assessed risk factors in 125 patients with ocular melanoma. Wearing sun glasses did not reduce risk. Lifetime UVB exposure was not associated with greater risk | Level IV |
| Vajdic [281] | Case control study of 290 patients with ocular melanoma. Total UVR exposure, especially prior to age 40 increases life risk of ocular melanoma | Level III.2 |

Table 3: Factors that increase UVR exposure whilst arc welding [276]

| Factor | Effect |
|---|---|
| Working close to arc | Radiation dose is inversely proportional to the square of the distance from the arc [282] |
| Increased Arc energy | Increases UVR |
| Duration arc is struck | Increases UVR |
| Increasing electrical current | Greater current produces increased UVR |
| Metal being welded | Aluminium arc welding produces high levels of UVR. Stainless steel welding produces intermediate levels. Arc welding iron produces still less UVR |
| Shielding gas used | Helium absorbs more UVR than argon. Shielding with helium thus reduces skin exposure to UVR |
| Angle of plate | Emission is maximum at 50 – 60 degrees from the surface of the plate being welded [282] |
| Welding with no arc | Other forms of welding produce minimal if any UVR. Non arc welding techniques include; oxy-acetylene welding, resistance welding, friction welding, laser and electron beam welding, friction stir welding |

Table 4: Factors contributing to the high levels of UVR emission when welding aluminium [283]

| Factor | Effect on UVR emissions |
|---|---|
| High Conductivity | Aluminium is 4 – 5 times as conductive as steel, requiring higher arc energy to concentrate sufficient power to effect a weld |
| Shiny surface | Aluminium is more reflective than steel |
| Technique required | Welders using high radiation techniques such as gas metal and gas tungsten arc welding |

Table 5: Welding processes and UVR emission produced by each [276] [283]

| Level of UVR emission | Welding processes |
|---|---|
| High | Gas metal arc welding Gas tungsten arc welding |
| Medium | Most arc welding processes including domestic units |
| Low | Submerged arc welding |
| Minimal or nil | Oxy-acetylene welding Resistance welding<br>Friction welding<br>Laser and electron beam welding Friction stir welding |

Figure 1: (welder hands.jpg)

Welder with multiple squamous cell carcinomata (SCC) on the hands despite denying a history of outdoor exposure. All five lesions marked were proven SCC on histology.

Figure 2: (welding tubes.jpg)

Tradesman using gas metal arc welding with a relatively high current. His unprotected left hand is very close to the welding arc. His head is closely over the arc risking welding fumes into his lungs.

Abstract:

Most skin cancers are caused by solar ultraviolet radiation (UVR) and it is believed that the most dangerous part of the UVR spectrum is Ultraviolet B (UVB) (315 – 280 nm). Fortunately, most of UVB is screened from the earth's surface by the outer atmosphere. Arc welding produces the full spectrum of UVR, including UVB. It is therefore likely that welders will be exposed to a greater risk of skin cancer than the rest of the population. Nevertheless, there has been minimal exploration to determine whether the UVR from arc welding is causing skin cancer.

The only major study of skin cancer from arc welding involved examining welders who were careful to protect themselves. The workers did not demonstrate an increased incidence of skin cancers in this study. Cancers may take years to develop and there was no follow-up of these workers to see if an increased incidence of cancers developed over time. Further, the radiation protection observed by these welders may not be typical of the welding industry as a whole. As such, the study cannot be extrapolated beyond this safe workplace and these young welders. Further studies are needed examining welders in their senior years, ensuring there is a lengthy time for their skin to have developed cutaneous malignancies. In contrast to cutaneous malignancies, there is evidence that welding increases the risk if ocular malignant melanoma. Just as we urge the public to protect themselves from UVR, we need to consider similar advice to arc welders.

Another manuscript alerting general practitioners to the possible large ultraviolet doses than can be endured while arc welding was published in “Australian Family Physician”.[238]

In May 2008[236] a short letter on melanoma update was published in the British Medical Journal. It reads as follows:

## *Sentinel lymph node biopsy: Let's get back to basics in managing melanoma*

I find the debate about sentinel node biopsy puzzling.[1] Clinicians are getting bogged down with this question while the fundamentals of managing cutaneous melanoma are being neglected. A recent Australian study[284] showed that doctors perform poorly in key aspects of managing this aggressive tumour.

Only a third of doctors excised cutaneous melanoma with the margins recommended by the Australian guidelines - a third used larger margins and, more worrying, a third used narrower margins. Most doctors failed to check the skin at follow-up, and they often diagnosed suspicious lesions by biopsy not local excision. Australian surgeons are slow to acquire dermoscopic skills that improve early diagnosis of melanoma. A patient with a thin melanoma is more likely to develop another cutaneous primary than metastatic disease. Yet dermoscopy and skin checks are often neglected.

If surgeons used time spent doing the sentinel lymph node biopsy in routinely examining the skin at follow up, there would be a tangible gain for our patients. In contrast, a procedure with a 10% incidence of complications[256] which does not improve five year survival,[285] is hardly a tangible gain.

Let us get back to the basics. Let's offer our patients skin checks for life, ensure dermoscopy is a routine part of this examination, and excise suspicious lesions rather than biopsy them to gain histology. Most importantly, let's give our patients with invasive melanoma a minimum 10 mm margin of normal skin rather than skimp.

Other published works in the field of skin cancer have also been completed, again not specifically related to complications of skin surgery.[244, 267, 286-288]

These publications have collectively provided further education and information for general practitioners managing skin cancer including the management and minimization of complications associated with skin lesion excision.

# Chapter 10 Conclusions

This thesis comprises seven original published studies.[122, 125, 141, 171, 177, 199, 204, 289] Supporting the seven substantive works is a number of other informative and educational published manuscripts.
The predominant conclusions of the seven trials are as follows:

1) Infection prospective study:

Our data suggest there are limited circumstances in skin lesion surgery where an infection incidence of over 5% could be expected. The area of greatest risk was below the knee. This includes the shin, calf foot and toes. Infection incidence was significantly higher below the knee than above the knee. There is a case for routine preoperative systemic antibiotics for all skin surgery procedures in this region.
Risks of antibiotic resistance would need to be considered in any decision to routinely administer antibiotics prior to skin surgery. Other circumstances where an infection incidence over 5% was noted include: wedge resections of lips and ear and skin grafts. Skin surgery in the groin may result in a similar increased risk. My data was too limited to make a conclusion in this region.
Skin flap repairs resulted in a fivefold increased incidence of infection compared with direct closure. Nevertheless, the only site where skin flap repairs resulted in an infection incidence of over 5% was below the knee. As such, expected closure is not, per se, an indication for preoperative antibiotic prophylaxis. This study was limited by a lack of multivariate analysis. Given multiple risk factors were apparent, such an analysis would have been preferable. Further, age was not considered as a possible confounder in this study.

2) RCT of ointment on wounds prior to dressings

There appears to be no value in applying ointment to wounds prior to occlusive dressing. Neither the application of sterile paraffin nor mupirocin ointment resulted in a significant difference in post operative complications. In particular, infection incidence was not altered by the administration of these agents. Pain, wound discomfort and aesthetic outcome were also not altered by usage of such a single application of ointment.
Of concern was an unexpected risk of skin necrosis in the mupirocin arm of my trial. Topical antibiotics can also result in contact dermatitis and antibiotic resistance. Topical antibiotics are contraindicated following the sutured closure of clean skin surgical wounds.

## 3) & 4) Retrospective trial of the reducing opposed multilobed (ROM) flap repair

The ROM flap is a novel flap for closures below the knee. Based on first principles it was designed to meet the ideal requirements to minimize complications in this at risk site.

The subsequent retrospective trial of ROM flaps demonstrated reduction in the incidence of end flap necrosis but wound infection was not significantly reduced with this technique. Overall, complication incidence was reduced when this repair technique is used to close defects 11 to 45 mm below the knee when compared with traditional closure techniques.

## 5) The effect of antithrombotics on post operative bleeding complications

There are limited circumstances when warfarin should be ceased prior to skin cancer excision. We identified four independent risk factors for bleeding following skin lesion excision: warfarin, age ≥ 67, surgery on or adjacent to the ear and closure by skin flap or graft. Only when 3 or more out of four risk factors are present can a post operative bleeding incidence of greater than 4% be predicted.

Given the life threatening thrombo-embolic sequelae that can follow short term cessation of warfarin, my data suggest it should not be routinely ceased for skin cancer surgery and should never be ceased within a month of a patient suffering deep venous thrombosis or pulmonary embolus. In general, my data shows short term stoppage of warfarin should only be considered when two or more further bleeding risk factors are present.

Care should be taken to ensure INR levels are within reference range and below 3.0 both prior to skin surgery and in the post operative period.

Aspirin was not demonstrated to be an independent risk factor for post operative bleeding and should not be ceased for skin lesion excision based on my data.

## 6) Body sites and bleeding risks

The ear and skin immediately adjacent to the ear is the only site where an increased incidence of bleeding complications can be predicted based on my data. Added care with haemostasis is needed when operating in this area. Most post operative bleeding complications can be managed conservatively and outcomes are invariably excellent following the interim setback. We found only one case in 2000 can one expect to have to reopen a wound to manage active bleeding in the post operative period.

## 7) Patient perceptions of their skin cancer surgery

The trunk is the only body site we identified where the aesthetic outcome of the wound was least accepted by patients.

Patients did not associate suffering surgical complications with a more adverse perception of the skin cancer service. Patients accept that complications can happen and this did not result in itself in a poor assessment of the skin cancer service.

In monitoring the quality of service provided, the surgeon needs to consider aspects of service beyond minimising tumour recurrence, minimising complications and addressing complaints if and when they are made.

If a patient feels his / her wound is less aesthetic than their expectations, we found they are more likely to consider the surgeon and the experience as suboptimal. Patients saw perceived overcharging, poorly explained pathology and waiting for surgery as problematic.

## 8) Findings and features that pertained to several studies:

We did not find that smokers or diabetics suffered increased complication rates compared with non smokers or non diabetics. However, the infection data was not multivariate and a further analysis with binary logistic regression would be useful to confirm that smoking and diabetes do not alter infection incidence in my data.

Bleeding complications and infective complications occur largely in different wounds in different locations. One rarely leads to the other.

Interestingly, patients taking warfarin, whilst at greater risk of post operative bleeding complications, were not at increased risk of post operative infection. We did not find any increased complication incidence in patients taking aspirin. Aspirin appears to be a safe medication that can be continued for skin surgery.

Two thirds of patients do not require analgesia following excision of skin lesion and those that require analgesia are predominantly controlled with paracetamol. Wound dressings are well tolerated by patients.

All of the studies undertaken were single institution studies involving a single surgeon in temperate southern Australia. This is a substantial limitation of all the studies undertaken. These findings might not be applicable to other clinicians in other locations and other climatic conditions.

## 9) Regions of the body:

We identified that different regions of the body are associated with different post operative complications.

Infection is greatest below the knee, bleeding is greatest on or near the ear, yet patients perceive wound outcomes the worst following surgery to their trunk. It was interesting that outcomes varied considerably in relation to the parts of the body being managed.

# Chapter 11 Where to from here?

This program of studies is not complete. Further studies in the program are in press, pending or envisaged.

### Further research questions identified:

The findings of all studies could be best validated by multi centre future trials involving more than one clinician and with more climates and circumstances involved.

Data on infection risk factors could be further analyzed using a multivariate approach. Age should be considered as a confounder in such an analysis. Diabetes and smoking as possible risk factors for infection should also be considered in such a multivariate approach.

Further studies could be undertaken with patients rather than lesions as the predominant subject for examination.

A future randomized controlled trial would be required to determine whether routine systemic antibiotics prior to skin surgery below the knee makes sufficient difference in post operative infection incidence to justify the antibiotic administration.

While we assessed mupirocin ointment on closed wounds, other antibiotic ointments were not trialled and there is prospect that other agents may provide a benefit that was not shown with mupirocin.

A further prospective randomized controlled trial of ROM flap closures below the knee would provide a greater level of evidence than the retrospective trial published.

It is often suggested that complications are linked to each other. For example, some suggest that haematoma often leads to abscess. Infection is also said to be associated with wound dehiscence. To date we have not specifically examined such linkages, though the database is robust enough to do so.

A further study looking at situations where multiple complications occur in single wounds could be drawn from the existing database. This would help identify whether patients who suffered a post operative bleed were more prone to infection than those who did not.

### Research with no funds:

It is noteworthy to reflect on the basis of the seven original studies that comprise this thesis. There was no University, Government, Corporate or any outside funding source for any of these studies. They were undertaken within the context of a small single doctor private medical practice. The costs to effect these studies were entirely borne by Dr. Anthony Dixon from revenue derived from his private practice of managing skin cancer. Even the mupirocin ointment required to effect the ointment study[125] was privately purchased from the local pharmacy.

Yet these publications comprise the largest, (by patient number) studies of infection, perception, skin flap and bleeding complication trials ever undertaken in dermatologic surgery.

## The Future:

Further studies are planned or have been completed to draw from the existing database. Such studies include:

**Do smokers fare worse than non smokers in skin surgery?** Our existing database suggests they fare no differently to non smokers. However, a multivariate analysis of smoking with respect to all complications has not been evaluated. My existing infection study[122] was univariate. We have now completed a multivariate analysis of data regarding our smokers and non smokers. This study has been published in the British Journal of Dermatology[290].

**Do patients with diabetes fare worse than non smokers in skin surgery?** Again my existing study regarding infection risk factors did not evaluate Diabetes as a risk factor with a multivariate approach[122]. My bleeding study was multivariate and found Diabetes was not predictive of post operative bleeding[177]. But what of other complications? We have completed a manuscript of Diabetes and skin surgery complications using a multivariate approach. This study has been accepted for publication by Dermatologic Surgery.

**Age and skin surgery complications?** We have identified that age over 66 is a predictor of bleeding complications[177]. But what of other complications? Age was not considered in my analysis of wound infections. Age may be predictive of infection and other complications. We envisage a further analysis of my data to specifically address whether or not age is predictive of any other complications.

**Does haematoma lead to infection? Does infection lead to dehiscence?** A close examination of patients with multiple complications within a single wound has not been explored. We envisage a further analysis and publication of skin surgery wounds that suffer two or more complications.

The program of seven studies completed within this thesis will drive further studies within this small private single doctor practice. The studies have substantially altered my practice with improvements for the benefit of my patients. We hope the studies may assist many practices. We hope it may inspire other doctors to initiate, effect and publish clinical trials within the context of their private practice. Clinicians can undertake research in their own small practice leading to large studies that are disseminated internationally for the benefit of all patients.

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# Appendices: Other publications

During the process of completing the trials within this thesis, other manuscripts were published with the intent of enhancing education and knowledge in skin cancer management.

Several of these were published in Australian Family Physician. These manuscripts are reproduced here in as published.

Appendix 1 Imiquimod of BCCs

Dixon AJ. Multiple superficial basal cell carcinomata--topical imiquimod versus curette and cryotherapy. Aust Fam Physician 2005;34:49-52.

Appendix 2 23 Golden Rules

Dixon AJ, Hall RS. Managing skin cancer--23 golden rules. Aust Fam Physician 2005;34:669-71.

Appendix 3 Infiltrating BCCs

Dixon A. One lump or two? A case study of infiltrating BCC on the nose. Aust Fam Physician 2006;35:505-6.

Appendix 4 Dysplastic naevus syndrome

Dixon A. Dysplastic melanocytic naevus syndrome. Aust Fam Physician 2006;35:601-2.

Appendix 5 Other health problems

Dixon A. Skin cancer in patients with multiple health problems. Aust Fam Physician 2006;35:717-8.

Appendix 6 Skin cancer below the knee

Dixon A. Managing skin cancer below the knee. Aust Fam Physician 2006;35:785-6.

Appendix 7 Metastatic melanoma

Dixon A. Melanoma with cutaneous melanoma secondaries. Aust Fam Physician 2006;35:871-2.

Appendix 8 Micronodular BCCs

Dixon A. Micronodular basal cell carcinomas. Aust Fam Physician 2006;35:965-6.

Appendix 9 High risk SCCs

Dixon A. High risk squamous cell carcinoma. Aust Fam Physician 2007;36:49-50.

Appendix 10 Arc welding and skin cancer

Dixon A. Arc welding and the risk of cancer. Aust Fam Physician 2007;36:255-6

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Appendix 11 Rare skin cancers

Dixon A. Rare skin cancers in general practice. Aust Fam Physician 2007;36:141-3.

Appendix 12 Bleeding complications in skin surgery

Dixon A. Managing bleeding complications in skin surgery. Aust Fam Physician 2007;36:435-6.

Appendix 13 Imiquimod for actinic keratoses

Dixon A. Treating actinic keratoses with imiquimod. Aust Fam Physician 2007;36:341-2.

# Multiple superficial basal cell carcinomata

## Topical imiquimod versus curette and cryotherapy

**Anthony J Dixon,** MBBS, DipRACOG, FACRRM, is a dermasurgeon and Director, Skincanceronly, Geelong, Victoria.
anthony@skincanceronly.com

**BACKGROUND**
Superficial basal cell carcinoma can be successfully managed by means other than surgical excision. Nonexcisional approaches include topical imiquimod, and curette and cryotherapy (C&C).

**OBJECTIVE**
This article discusses the management of an insulin dependent diabetic man aged 52 years presenting with 17 torso basal cell carcinomas (BCCs); mostly superficial BCCs (SBCCs).

**DISCUSSION**
Half were treated with topical imiquimod. The remaining lesions were treated with curette and cryotherapy. All lesions resolved with proven histologic clearance. The patient considered C&C caused him less discomfort and disruption. He developed a late secondary infection in some sites treated with imiquimod. At 12 months there was no evidence of recurrence though new nodular BCCs and SBCCs had developed elsewhere on his upper torso. He has elected to have future SBCCs managed with C&C. While excisional surgery remains the benchmark management for nonmelanoma skin cancer, topical imiquimod and C&C are important options for treating SBCCs.

**Case history**

PF, aged 52 years, is an airline engineer and an insulin dependent diabetic. He presents with a large ulcerating nodular basal cell carcinoma (BCC) on his right leg. A wound infection followed its excision. Examination of his skin elsewhere revealed 17 further BCCs located on his pectoral, trunk and arm regions. He was keen to explore nonexcision treatment for these BCCs.

## Treatment options for BCC

### Topical imiquimod

In the largest trial of topical imiquimod for superficial basal cell carcinomas (SBCCs), Geisse[1] demonstrated 82% histologic clearance rate when applied five times per week. This is in keeping with earlier studies.[2,3] Imiquimod also has a role in treating large and long standing SBCCs.[4] Limited experience managing nodular BCCs with imiquimod has failed to demonstrate satisfactory clearance rates.[3]

Side effects are not uncommon and include erythema, scabbing, oedema, induration, itching, pain, erosion, and secondary infection. Pain varies with frequency of application.[1–3]

Following imiquimod treatment the skin can have an erythematous and slightly thickened appearance. Unfortunately, SBCCs can have a similar appearance. Superficial BCCs on the torso are often misdiagnosed as an inflammatory skin condition; malignancy considered only after the 'rash' fails to respond to topical corticosteroid and/or antifungal management.

### Curette with cryotherapy

Curette with cryotherapy (C&C) is an established approach to managing SBCCs.[5] Kokoszka[6] undertook a meta-analysis of treatment of BCCs with cryotherapy showing cure rates of around 90%. Most studies excluded difficult BCCs such as recurrent and morpheaform tumours. Many authors recommend curettage before cryotherapy as it defines and debulks the tumour. I favour this approach using a blunt curette, cleaving the BCC in one direction before a second curettage cleaving perpendicular to the first. A blunt dermal curette is cheap, able to be sterilised and reused.

Bleeding may be a problem following curettage. Spot monopolar electrocautery is my preferred approach to this predicament. Haemostatic dressings can also be used.

**Table 1. Summary of managing SBCC with surgery versus imiquimod versus C&C**

| | Surgical excision | Topical imiquimod 5% | Curette and cryotherapy |
|---|---|---|---|
| Recurrence rate | 5% or lower with experience | Around 20% | Around 10% |
| Pain | Not often a problem. Oral paracetamol for a few days meets needs of most | Varies with frequency of application and can continue for 6 week duration of treatment | Typically uncomfortable for a week or so |
| Cost to patient | Gap payment above Medicare for surgery item numbers | Expensive script. Many scripts may be needed to treat multiple/ large SBCCs | Gap payment for curette item numbers |
| Scarring | Generally least, though wound spread, hypertrophy and keloid can be issues on the upper torso | Usually noticeable post-treatment, but keloid and wound spread not considered issues | Hypopigmentation or discolouration may occur |
| Experience required by treating doctor | Large wounds on the upper torso may need deep sutures and/or flap repairs to ensure satisfactory outcomes including acceptable wound spread incidence | Skills recognising the erythema and induration associated with treatment are required, enabling suitable counselling to patients. A treatment 'break' often helps distressed patients | The physician needs to learn the feel of using a skin curette, identifying the different character of scraping friable SBCC tissue versus normal underlying dermis |
| Histology | Mandatory | Strongly recommended in all cases. Clinical diagnosis is insufficient | Always send any curetted tissue for histologic confirmation |
| Bleeding | Haemostasis required at time of surgery. Postoperative bleeds can occur | Not an issue | Control spot bleeds with diathermy or haemostatic dressings |
| Keloid prone patient | Avoid surgery, especially on torso | Recommended (imiquimod is being used by some to treat keloid) | Less keloid risk than excision |
| Healing time | Predictable | Six weeks plus, due to effects of imiquimod locally | Predictable and prompt |
| Patient involvement in own treatment | Usually minimal | Involved with ointment application and wound care | Usually minimal |
| Nodular BCCS | Treatment of choice | Contraindicated Recurrence rates unacceptable | Not recommended for difficult BCCs such as morpheaform, ulcerating and sclerosing BCCs |
| Recurrent BCCs | Excision required. Referral for Mohs micrographic surgery should be considered | Contraindicated based on evidence to date | Contraindicated based on evidence to date |
| Face and ears | Treatment of choice. Scars on face generally less noticeable than on torso | Avoid. Very little data. Not endorsed for face | Avoid as pigmentation changes can be more noticeable than surgical wounds |
| Anticoagulants | Increased bleeding risk. Extra care with haemostasis. Ceasing warfarin/ aspirin in advance is no longer common in cutaneous oncology | Must be considered given the absence of bleeding issues | Haemorrhagic blistering can occur. More care needed with spot diathermy |
| Dark skinned patients | Caution. Keloid formation or poor scarring can be accentuated | Must be considered given minimal keloid and hypopigmentation concerns | Avoid. Hypopigmentation can be striking and distressing to patient |
| Very large SBCC | Surgery could be major with large scarring | Can be used on even large SBCCs | Very useful technique, even on flexural regions |

Cautery should be minimal as it is associated with more scar risk than curette and/or cryotherapy. I no longer treat nonmelanoma skin cancer (NMSC) with curette and broad based cautery in view of these scar risks.

Reported complications of C&C include ulceration, hypopigmentation, blistering, scarring, oedema, pain, secondary infection and recurrence.

## Surgery

Excisional surgery generally produces less pain, quicker healing and more aesthetic scars than less invasive alternatives. Most authors only recommend nonexcisional approaches for managing simpler BCCs. Indeed, SBCC is the only skin cancer for which imiquimod treatment is approved in Australia. National Health and Medical Research Council guidelines[7] regard surgical excision as the 'gold standard' for management of NMSC against which nonsurgical treatments should be judged.

Nonsurgical approaches to managing SBCCs are reserved for when surgery is considered inappropriate. Excision is often more convenient for patients with fewer visits to the doctor and less self management of the wound.

## Management of patient

Every lesion on PF's body suggestive of NMSC was numbered and punch biopsied (*Figure 1, 2*). Nineteen biopsies revealed 17 BCCs, mostly SBCCs. Lesions eight and 10 were actinic keratoses and treated with cryotherapy, BCCs one through seven and nine were treated with C&C. This included all back lesions given the logistics of accurately applying cream to these sites, BCCs 11 to 19 were treated with imiquimod.

Lesions selected for C&C were curetted until no apparent tumour remained. The base and 4 mm of surrounding skin was then treated with a 15 second freeze/120 second thaw/10 second freeze liquid nitrogen cryospray. Moist occlusive dressings were then applied to each site. PF was instructed to carefully apply imiquimod 5% w/w cream accurately and very sparingly, 4 days per week for 6 weeks to the sites selected for imiquimod therapy. Following Geisse's[1] study, five applications per week for 6 weeks is now the generally recommended regimen.

At 2 weeks, PF commented that the imiquimod sites were very itchy, especially his left shoulder (*Figure 3*). Discomfort was most marked an hour after application. Pruritus subsided 24 hours following application. Some sites treated with C&C bled for up to 2 days following treatment; sites were all uncomfortable for 3–4 days.

Three weeks later PF complained of increased imiquimod site pain, swelling, lethargy, fever and generally feeling poorly. He had impetigo with tender left axillary lymphadenopathy. Oral dicloxacillin resolved his skin infection. At this stage (week 5), all his C&C treated sites were healed (*Figure 4*) and he commented that he had been 'no longer aware' of these sites since week 2.

## Results

At 6 weeks, each site was biopsied confirming no evidence of residual BCC at any site. At 10 weeks all sites felt the same to PF and looked clinically indistinguishable (*Figure 5*). PF considered that the problems he experienced with imiquimod treatment would ensure he chose C&C to manage future SBCCs. Note that despite *Figure 2* demonstrating BCCs and *Figure 5* demonstrating resolved BCCs, both present as similar erythematous macular regions on his torso. This further highlights the difficulties that can be experienced in diagnosing SBCCs.

At 6 months follow up, PF had developed two new SBCCs. One had developed in the right pectoral region where similar lesions had been treated with C&C (*Figure 6*). The other SBCC had developed in the left (imiquimod) pectoral region. Both were treated with C&C.

At 12 month follow up, two new nodular BCCs had developed, again one on each shoulder. Both were surgically excised (*Figure 7*). Follow up to 12 months therefore demonstrated an equal propensity to develop BCCs in the regions treated with each modality. These new BCCs were at new sites on his torso. They were not recurrences of previously treated lesions.


**Figure 1. Upper back with multiple SBCCs numbered – note previous scars from previously excised skin tumours**


**Figure 2. Chest and arms. All but lesions numbered 8 and 10 are BCCs**

**Figure 3. Two weeks into treatment. Note scabs on C&C sites and erythema at imiquimod sites**

**Figure 4. After 5 weeks. C&C sites healed. Secondary impetigo affects some imiquimod sites**

Figure 5. Ten weeks following clearance biopsies

Figure 6. Left shoulder. One of two new nodular BCCs that developed 6 months post imiquimod/C&C treatment. The other nodular BCC developed on the right shoulder

Figure 7. At 12 months, two further superficial BCCs had appeared on the left and right pectoral regions

## Discussion

Each of PF's 17 truncal, pectoral and arm BCCs were successfully treated with either C&C or topical imiquimod. Following treatment, all sites settled and the final cosmetic results were indistinguishable. Neither treatment prevented new BCCs developing in nearby sites. Recurrence remains a possibility. Given the extent of his BCC disease to date, further tumours are very likely. Given the data to date, PF was fortunate to have histologic clearance of all tumours.

PF will choose C&C to manage future SBCCs. In my experience, many patients find the lengthy 6 week discomfort that can be associated with imiquimod treatment to be tiresome. Other patients are much happier applying a cream than having their skin 'scraped and frozen'. Many find imiquimod treatment to be very effective without the adverse effects noticed by PF. A summary of further differences between imiquimod, excision and C&C is outlined in *Table 1*.

In special circumstances, these less invasive treatments may have a more prominent role, eg. young people, high keloid prone patients, diabetic patients, those with numerous tumours, immunosuppressed patients, those on warfarin, or those with a pacemaker. In these circumstances, the clinician may seek to avoid excisional surgery.

## Conclusion

Excisional surgery remains the benchmark by which all skin cancer management must be compared. Both C&C and topical imiquimod treatment are effective means of managing superficial BCCs and should be considered in patients with multiple superficial BCCs. Clearances rates with imiquimod are around 80% versus 90% with C&C.

Conflict of interest: none declared.

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AFP

**Correspondence**
Email: afp@racgp.org.au

# Managing skin cancer

## 23 golden rules

**Anthony J Dixon,** MBBS, DipRACOG, FACRRM, is a dermasurgeon, and Director of Research, Skin Alert Skin Cancer Clinics, Geelong, Victoria. anthony@skincanceronly.com

**Richard Scott Hall,** MD, is a dermasurgeon, Cookeville Regional Medical Centre, Cookeville, Tennessee, USA.

From their collective experience in Australia and the USA, dermasurgeons Anthony Dixon and Scott Hall have compiled a list of 'golden rules' for general practitioners to help reduce errors and problems with skin cancer management. It is anticipated that these tips will provide a brief yet informative reference when faced with skin cancer management concerns in general practice.

### 1. Suture rule – if histology indicates further treatment is needed, leave sutures in

If histology reveals that more surgery is needed, don't remove sutures. They are a marker of the location and direction of the initial surgery. One does not need to worry that sutures left a long time might cause a reaction – the skin is set to go in subsequent surgery. Early suture removing can lead to later head scratching!

### 2. Melanoma rule – cut it out early and cut it out widely

Only two things have been demonstrated to improve outcome/survival for melanoma patients: cut it out early and cut it out widely. In short, chemotherapy, radiotherapy, lymph node dissection, sentinel node biopsy, immune therapy, BCG therapy and anything else tried has not been demonstrated to improve patient outcome/survival.

### 3. Basal cell carcinoma rule – BCCs ain't BCCs

There are three broad groups of basal cell carcinoma (BCC):

- superficial BCCs (SBCCs)
- simple nodular BCCs, and
- tough BCCs (*Figure 1*).

The latter include morphoeic, desmoplastic, recurrent, and micronodular BCCs, as well as those previously partly treated with cryotherapy many times or photodynamic therapy (PDT). Other than surgery, options for SBCCs include imiquimod ointment, curette, cryotherapy and PDT. We would never consider these options for tough BCCs. In contrast, Mohs surgery is benchmark management for tough BCCS, but elaborate overkill for SBCCs.

### 4. Squamous cell carcinoma rule – SCCs can spread

Invasive SCCs can go to nodes and further. Squamous cell carcinomas at greater risk of spread include:

- recurrent SCCs
- tumours on lip, ear and scalp
- large tumours, and
- aggressive poorly differentiated or spindle malignancies.

Think beyond 'cut it out early and cut it out widely' with these tumours.

### 5. Dysplasia rule – dysplastic naevi need to be diagnosed (not necessarily excised)

A patient with multiple dysplastic naevi is at high risk of developing malignant melanoma. However, removing the dysplastic naevi does not remove the risk. The melanoma is more likely to develop elsewhere on skin that now

**Figure 1. Patient with two seemingly innocuous actinic keratoses on the right side of the nose. They were in fact linked under the skin as a large morphoeic BCC, requiring Mohs surgery**

looks 'normal'. The emphasis of treatment is photography, surveillance and dermoscopy, not excising everything looking dysplastic.

### 6. Hole rule – think first of the mole, next of the hole

Recurrence rates are the key outcome indicator in cutaneous oncology. The biggest factor leading to high recurrence rates is surgery with inadequate margins. First work out what margin each tumour needs. Then work out whether you will be able to close that defect, or refer the patient.

### 7. Examination rule – with bright light and magnification, less tumours will be missed

The jeweller's loupe, natural light and good artificial lighting, all help the close examination of suspicious skin lesions. A digital camera and a dermoscope are also vital tools. Patients often ask you to glance at a lesion at the end of a consultation on another matter. Avoid the temptation to have a quick glance with poor lighting and no equipment. A melanoma will not be found if it is not carefully looked for.

### 8. Dermoscopy rule – dermoscopy diagnoses dark dudes

Accuracy in diagnosing melanoma and other dark skin lesions improves dramatically with dermoscopic skills (*Figure 2*). This means having a dermoscope at the ready, and using it repeatedly to build familiarity. Education on what to look for will enhance skills and accuracy. Further, even when the dermoscope does not provide the answer, it often helps to decide whether a punch biopsy, shave biopsy, curette or excision is appropriate. Large brown macules are often best shaved; this way you sample widely without a full thickness scar. Don't simply freeze undiagnosed pigmented lesions. Remember 'ABCD' with pigmented lesions: Asymmetry, Border, Colour, Diameter.

**Figure 2. This small lesion had suspicious features on dermascopy: blue-white veil, pseudopods and dots and globules throughout the lesion. The patient had recently been examined by a 'skin cancer detection machine' and advised that he did not have a melanoma (see *Rule 15*)**

### 9. Histology rule – send it to the lab, not the bin

Among others, medical defence organisations warn us against treating skin cancer without histology. Surprises happen (*Figure 3*). Some malignant melanomata look nothing like melanoma. If every specimen goes to histology, many surprises can be discovered. If the pathology report seems odd, consider another biopsy. A commonwealth agreement means extra histology does not increase government spending on histology. If in doubt, have little hesitation in sending specimens for histology.

### 10. Nerve rule – perineural invasion on histology means radiotherapy consult

Perineural invasion is an important warning sign on histology reports. Tumour can 'skip' down the nerve. This means that a tumour may have continued well beyond histologically clear margins. Options include further surgery and radiotherapy. Where a radiotherapy service is available, offer it to the patient.

**Figure 3. Apparent epidermal cyst ready for excision. Histology revealed a dermal melanoma**

### 11. Follow up rule – examine rest of skin

In following up a skin cancer patient, the most important aspect of the consultation is examination of the remaining skin. Melanoma patients have a high risk of a second tumour. A patient who has had one nonmelanoma skin cancer has a two out of 3 chance of developing another. A patient who has had three skin cancers nearly always grows more skin cancers – and the next might be malignant melanoma.

### 12. Research rule – we are supposed to be scientists

While adjuvant therapy for melanoma is limited thus far, we can't find that breakthrough unless current and future ideas are trialled. Many tertiary centres in Australia are trialling future melanoma treatments. In the meantime, as scientists, we must be prepared to cease techniques that were once popular and have been found wanting in more recent larger long term trials.

### 13. GP rule – GPs rule!

Most skin cancers in Australia are managed by GPs. Australian GPs are among the best doctors in the world at recognising skin cancer. Further, GPs know when lesions are beyond their expertise and other doctors need to be involved. Patients need to have the advice and confidence that their own GP is the doctor they should see to have their skin checked and skin cancers treated, and that their GP knows exactly who is best to treat them if their skin cancer is too difficult.

### 14. Photography rule – two or more: number and photograph them

Photography is increasingly useful in cutaneous oncology. Quality digital photography is affordable and images can be easily downloaded into clinical software. When removing or sampling many lesions, photography becomes invaluable. Mark the skin and photograph each lesion in advance (*Figure 4*). Remove them in order as numbered. When histology returns, it becomes easy to determine which report relates to which anatomical site.

**Figure 4. Skin lesions numbered and photographed before excision**

**Figure 5. Persisting 'pink pimple'. This lesion persisted for several months, slowly enlarged and became irregular. Histology revealed a nodular melanoma**

### 15. Computer rule – an Australian GP beats any machine at diagnosing skin cancer

There are numerous computer programs claiming to diagnose skin cancer by linking software to a scanner (*Figure 2*). They are heavily marketed to the public, especially in Queensland and New South Wales. Slogans such as, 'Be scanned be sure' are grossly misleading. Patients are better off seeing their own GP (see *Rule 13*).

### 16. Experience rule – the more we see and treat, the better we get

Accuracy in skin cancer management comes with experience. The best are those who see and manage the most. Unlike most areas in medicine, we have a constant 'supervisor' continually checking and rechecking our skill and accuracy on everything we do in cutaneous oncology. It is called histology. Take a stab at the diagnosis every time and write it down in the notes. The learning never stops.

### 17. Dressing rule – wounds heal better occluded

Sutured wounds have better cosmetic outcomes if covered with an occlusive dressing for at least 4 days. Uncovered wounds have more scab formation, more infection and worse scarring. Cover every wound and urge the patient to keep the dressing on as long as possible. The wound may 'smell' when the dressing is removed. Smell is not infection.

### 18. Time rule – if you only ask one question, make it: 'How long has it been there?'

'Months' is the key. Changes or growth over days or weeks are often due to inflammation. It may soon change back or disappear. If it has not changed for years then it probably won't change any time soon. If the patient says the lesion is changing or growing and staying changed for months, be quick to biopsy.

### 19. Orientate rule – mark or stitch one edge of tumour for orientation purposes

It is unfortunate when histology says, 'incompletely excised at one lateral margin'. It helps when that margin can be identified. A 'nick' or stitch at one point can be denoted 12 o'clock for pathology. The report back from histology might then say, 'incompletely excised at ## o'clock'. The result is the affected margin can be identified and addressed without having to excise further in every direction.

### 20. Pink rule – persisting pink 'pimple' might be nodular melanoma

Nodular melanoma accounts for 15% of malignant melanoma, but 50% of melanoma deaths. They are often amelanotic and difficult to diagnose. Many are described as a pink pimple that grew and didn't go away (*Figure 5*). Nodular melanomas do not have classic dermoscopic features. A short fuse to histology is essential.

### 21. Efudix rule – GPs pick lesions for Efudix, not patients

5-fluorouracil (Efudix) is used for benign actinic lesions, not skin cancer. Never prescribe 5-fluorouracil for self administration by the patient. This can lead to nightmare malignancies. It should only be prescribed after careful examination by a physician to rule out existing cancers. Treat only for a specified period under close medical supervision.

### 22. Location rule – tumours on eyelids, nose and ear require considerable expertise

Banal looking tumours in bad locations can require aggressive and disfiguring treatment to save vital structures and/or life. Consider referring BCCs located near the nose, ears and eyes. Even small BCCs can invade the nasal vault or the orbital rim. Orbital rim involvement is very dangerous and difficult to treat. Basal cell carcinomas on the ear can be much larger than apparent. For SCCs be aware of the temples, around nerve foramens such as the infra-orbital nerve and pre-auricular areas. They can be much larger or deeper than clinically suspected.

### 23. Curette rule – careful technique produces best results when curetting SBCCs or Bowen tumours

When treating a skin malignancy with curette, scrape from multiple angles, otherwise some edges will get less pressure. Curetting a BCC needs a sharp curette that you 'trust' as it lifts off the tumour. Continue until normal tissue is 'felt', even if the naked eye suggests otherwise. Consider cryotherapy to help destroy residual tumour cells following curettage.

Conflict of interest: none declared.

AFP

**Correspondence**
Email: afp@racgp.org.au

# One lump or two?

## A case study of infiltrating BCC on the nose

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

### Case history

A woman aged 42 years, who works as a hairdresser, presents with two apparent actinic lesions on the right of her nose (*Figure 1*).

Close clinical examination reveals the lesions are likely to be infiltrating basal cell carcinomas (BCCs). The lesions are firm with similar nontender indurations surrounding each site. Infiltrating BCCs can extend beyond the poorly defined clinical borders.

Could these two lesions be the one tumour?

Figure 1. Two nose lesions, highlighted by black pen

**The upper basal cell carcinoma (BCC) is approached first. Given the difficulties determining tumour border, this BCC is managed using micrographic surgery, a margin control approach sometimes termed 'Mohs' or 'slow Mohs' surgery (*Table 1*). In this technique the excision specimen is sent for urgent paraffin or frozen section examination. The defect is not closed until there is confirmation of margin clearance. This produces minimal recurrence rates in BCCs that would otherwise result in unacceptably high tumour recurrence risk. A critical aspect of this approach is careful mapping and orientation of the specimen (*Figure 2*). If further excision is required, one must be confident of the exact site on the patient's face.**

Histology demonstrates BCC extending inferiorly, confirming these two lesions are in fact a single BCC. Second stage slow Mohs is undertaken the day after the first stage excision. This involves excising the entire lower lesion and extending the dissection to include the involved border of the first stage excision. The defect following this second stage is shown in *Figure 3*.

Histology confirms the tumour is now fully excised. This leaves a sizeable defect to be filled. The major part of this defect is closed using a forehead flap. This flap is based on the contralateral supratrochlear artery.

### Table 1. Mohs micrographic surgery

Mohs micrographic surgery is an established benchmark method of managing difficult nonmelanoma skin cancer.[1] Its usage is typically for difficult BCCs on the head and neck. The tumour may be selected for Mohs surgery because it is a morphoeic, micronodular, or infiltrative BCC, because it has poorly defined margins, or because it is recurrent

BCCs previously failing treatment with other modalities such as imiquimod, photodynamic therapy, curettage, or cryotherapy are often selected for Mohs surgery because the previous treatment clouds determination of where residual tumour starts and stops

Sites where Mohs surgery is most often considered are:

- eyelids
- nose
- ear
- lips, and
- areas of the face near these organs

Classic Mohs micrographic surgery involves frozen section histology whereby the surgeon is also the histologist. Further sections are taken the same day until clearance is confirmed. This is frequently undertaken by dermatologists who have completed a post fellowship Mohs training program over 1–2 years

In 'slow Mohs' surgery, the dermatopathologist and surgeon work in partnership, and stages may take place over several days

Mohs surgery is readily available in most areas of the United States. In Australia the service is limited to a small number of major centres. General practitioners and patients would benefit from establishing if there is a Mohs or slow Mohs service in their area

Figure 2. Layout for first stage margin control surgery

Figure 3. Post second stage excision

Figure 4. Post first stage repair

Figure 5. Post second stage repair

Figure 6. Seven months after second stage repair

The flap folds down onto the nose (*Figure 4*). The patient must wear this 'trunk' across her nose for 2–3 weeks. Considerable preoperative counselling is required regarding the unsightly trunk.

The trunk is excised during the final stage of surgery (*Figure 5*). Note that the upper part of this defect has been left to heal by secondary intention. Secondary healing can be effective in certain circumstances. Concave regions with a firm base lend themselves to secondary healing. Classic sites where secondary healing may be considered are:

- conchal bowl of the ear
- near the inner canthus, and
- the lower leg.

Seven months later, the area has healed reasonably for a large defect (*Figure 6*). A 'web' of skin near the canthus may result from allowing this area to heal by secondary intent. This can be later revised.

## Summary of important points

- Infiltrating BCCs can appear with the majority of the tumour hidden under apparently normal looking skin.
- Where two new BCCs appear close to each other, consider they may be one tumour.
- Where borders of BCCs are impossible to clinically determine, consider micrographic controlled surgery.
- Secondary intent healing can be effective in certain circumstances. Concave regions with a firm base lend themselves to second intent healing.
- Skin grafts are now rarely used on the nose. An array of flaps invariably produce more acceptable results.
- Management of BCCs with cryotherapy, imiquimod, or fluoruracil cream (rather than obtaining histology), could lead to delay in diagnosis while the large deep tumours invade further into the nose and risk vital structures.

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Dysplastic melanocytic naevus syndrome

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case history**

Mr BS, 55 years of age, presented with numerous naevi in 2001. His history included a 0.85 mm thickness Clarke 3 malignant melanoma excised from his scalp at 50 years of age.

Initial examination revealed dozens of likely dysplastic melanocytic naevi (DMN) on his skin, especially on the trunk. The diagnosis of dysplastic melanocytic naevus syndrome was confirmed when several of the most concerning naevi were biopsied for confirmatory histology. Mr BS also demonstrated numerous pigmented seborrhoeic keratoses, many of which were quite dark and irregular. There was no evidence of any residual or recurrent melanoma.

**Dermoscopy of his dysplastic melanocytic naevi (DMN) showed pigment patterning that was often disrupted with brown dots frequently seen erratically placed through a naevus. Many of the DMN were irregular in shape, asymmetric, had variable colouration and had borders that were at times sharply defined and at times poorly defined. Mr BS therefore has two significant risk factors for the development of a second primary melanoma: a past history of melanoma and DMN syndrome.**

Digital dermoscopic images of Mr BS's remaining DMN were taken. He also had digital clinical photography of most of his skin demonstrating the existing lesions. Dermoscopic images were labeled with numbers on the body photographs. All photographs were stored on his computer medical record file.

Mr BS was reviewed every 4–6 months and his skin was examined with reference to his baseline photographs and digital dermoscopic images. His recorded DMN remained similar in appearance from examination to examination. In April 2005, the dermoscopic view of a lesion on his abdomen had changed significantly when compared to an image recorded 4 months earlier. The lesion had grown in a medial direction, with the new component to the lesion being dark and displaying disrupted pigment patterning. There were also some peripheral dots and globules appearing in the lesion and the suggestion of radial streaming. *Figure 1* shows a dermoscopic image of Mr BS's naevus in late 2004. *Figure 2* shows the same naevus in April 2005. *Figure 3* shows Mr BS's abdomen in April 2005. The changing lesion is just to the right of the umbilicus.

Figure 1. Dermoscopic image in late 2004

Local excision confirmed that this lesion was a second primary superficial spreading melanoma. It was an early Clark 3, Breslow 0.5 mm thick melanoma. This was subsequently widely excised with a 10 mm minimum margin (*Figure 4*).

Ongoing management will focus on the early detection of any further primary melanoma. If Mr BS is to die from metastatic melanoma, it will most likely be a melanoma not yet present on his skin but one that was delayed in diagnosis and management. He will need regular careful ongoing examinations, both of his existing DMN and any new lesions that develop. This surveillance should be undertaken by a clinician very familiar with dermoscopy and with access to clinical photography.

## Summary of important points

- A patient with five or more DMN has a >40 fold risk of developing melanoma.[1] Management centres on surveillance of the skin with clinical photography and dermoscopic imaging.[2]
- DMN syndrome is sometimes inappropriately managed by removing all the DMN. Melanoma

Figure 2. Dermoscopic image in April 2005

Figure 3. Abdomen showing lesion to the right of umbilicus

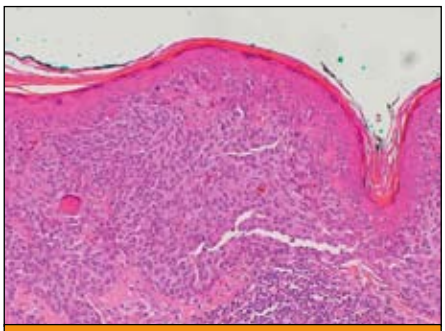

Figure 4. Irregular proliferation of atypical spindled melanocytes in the dermis and epidermis. The cells show no downward maturation and at the base of the lesion is a lymphocytre infiltrate

Figure 5. Typical dermoscopic appearance of a malignant melanoma

## Dermoscopy of melanoma

While Mr BS's superficial malignant melanoma did not demonstrate classic dermoscopic features, the clear change resulted in biopsy and diagnosis. In contrast, *Figure 5* shows numerous dermoscopic features of malignant melanoma including scar-like depigmentation, thickened and disrupted pigment patterning, and radial streaming. Note that within the lesion there are regions coloured: white, red, grey, black, brown and blue. In this case histology confirmed an obvious clinical dermoscopic diagnosis.

Recording a dermoscopic image does not need expensive equipment. Cheap readily available commercial digital cameras can be attached to inexpensive dermoscopes. The images can be downloaded into computer based medical records already in place in most Australian general practices. An outlay of $2000 will provide a practice with the dermoscope and camera to record dermoscopy on existing software (*Figure 6*).

Figure 6. Digital camera and dermoscopes

frequently develop in areas of the skin previously not demonstrating dysplastic naevus. Removing all a patient's DMN still leaves the patient at high risk of subsequent melanoma development.

- While DMN can be watched rather than excised, a changing DMN should lead the clinician to consider excision.
- Use of dermoscopy will improve diagnosis of melanoma while reducing the number of benign lesions excised.[3]
- General practitioners wishing to improve their skills in skin cancer management should consider dermoscopic training. As little as 4 hours of dermoscopy training has been shown to significantly enhance the skills of GPs in detecting melanoma.[4]
- Pigmented seborrhoeic keratoses are usually characteristic, but at times diagnosis is unclear. A biopsy is needed when melanoma cannot be excluded. A large study demonstrated that 0.66% of removed seborrhoeic keratoses were melanoma.[5] Document photographs and dermoscopic images of all seborrheic keratoses that are sufficiently suspicious to require histology.

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Skin cancer in patients with multiple health problems

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

## Case history

Mrs OL, 84 years of age, and living in an aged care facility, developed a nodule on her left cheek. She had a history of numerous past skin cancers, dementia, hypertension, epilepsy, and cerebrovascular accidents. Her memory was poor. Given her background health, the initial decision was made not to intervene with her left cheek lesion.

However, the tumour rapidly progressed over 1 year (*Figure 1*). It became chronically infected and resistant to antibiotic treatment and regular toileting. The soft friable surface of the tumour bled on contact and required constant dressings. The surface of the tumour had swirls of pink and red. There was no crusty keratotic surface. The border of the tumour was very sharply defined (*Figure 2*). The persistent offensive odour from the tumour resulted in other residents being unhappy to dine with Mrs OL. To keep the peace she ate alone in her room; eventually spending the majority of time in her room. She enjoyed her hair being styled but unfortunately the hairdresser would no longer attend her. Mrs OL's husband continued to visit her regularly. Loneliness and depression became issues with her ongoing isolation resulting from her visually offensive and malodorous tumour.

It was clear the tumour needed to be excised, primarily to allow Mrs OL to rejoin her friends and previous lifestyle. Her family requested that as much of the management as possible be undertaken on site in her own environment.

Figure 1. Chronically infected tumour

Figure 2. Tumour showing sharply defined border

**Surgical excision and a transposition flap repair was undertaken in the rooms with local lignocaine and adrenaline as the anaesthetic choice. Despite initial anxiety, Mrs OL coped well with the procedure.**

Histology confirmed a poorly differentiated squamous cell carcinoma (SCC). Margins were clear. The wound healed promptly and the offensive odour ceased. Mrs OL returned to her previous lifestyle and was again able to have her hair styled.

Surgical follow up at the aged care facility provided the complete picture of the impact of this excision on her lifestyle. The result at 3 months was encouraging (*Figure 3*). Two years on there was no evidence of recurrent tumour and Mrs OL was progressing well.

### No treatment

There are times when the appropriate management of nonmelanoma skin cancer (NMSC) is to leave them. Consider an elderly patient with Bowen disease or superficial BCC below the knee. You may consider that other health issues are likely to influence the patient's wellbeing long before the NMSC has any influence other than its appearance (which may not concern the patient). Simpler treatments such as cryotherapy and curettage can result in chronic infection and ulceration and may result in a greater disability for the patient than the NMSC was likely to produce if left alone.

Figure 3. Patient 3 months after surgery

## Summary of important points

- The decision to treat or leave can be difficult in patients with multiple health issues. The patient's general practitioner is well placed to balance the cutaneous oncology considerations with other health issues.
- 3 mm margins rather than wider margins were effected in the surgical management of this tumour. The emphasis was on returning the patient to her lifestyle rather than maximising long term survival.
- Skin cancers on the face have considerations in management well beyond the risks of local and systemic invasion. An unsightly tumour can have a major impact on daily activity. If it also has an offensive odour, treatment is imperative.
- Poorly differentiated SCCs look and behave very differently to well differentiated SCCs – they lack the crusty hard surface and can spread.[1] Metastatic potential is greater in these soft red tumours especially if >2 cm in diameter.
- Nursing resources involved in managing a tumour can influence the decision to treat a patient. In this case, frequent dressings and toileting were required by a stretched nursing staff. Following a relatively simple surgical procedure, nursing time was then available for meeting other needs of the resident.

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Managing skin cancer below the knee

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mr RR, 74 years of age, developed a nodule on his lower right leg in mid 2005. He was offered the option of excision, skin graft and 10 days bed stay with elevation at a private hospital, but declined due to the cost. He was then referred to a major urban cancer institute for opinion. He was advised that the nodule would most likely fall off and that a 'watch and wait' approach was indicated. Presumably there was a clinical diagnosis of keratoacanthoma.

**The nodule continued to grow and he became disillusioned. He asked for referral for a third opinion. I then saw him some 3 months after his first assessment. He demonstrated a large friable lesion 27 mm across at its maximum diameter (*Figure 1*). There had been no biopsy taken up to this point. I aggressively debulked the lesion including all apparent pathologic tissue. Histology confirmed squamous cell carcinoma (SCC) (*Figure 2*).**

He had ipsilateral inguinal nodes on presentation. Fortunately these were reactive and settled with antibiotics.

Being a keen amateur photographer, Mr RR had captured the tumour at various stages in its growth. *Figure 3* and *4* show the tumour 8 weeks and 2 weeks before my assessment.

Following histologic confirmation, the SCC was widely excised. There was no residual tumour on histology. The defect was closed with a reducing opposed multilobed (ROM) flap repair (*Figure 5*). This closure technique produces better outcomes than traditional flaps and grafts for medium sized defects below the knee.[1] As is usual following ROM flap repair, Mr RR was mobilising the same day. He was advised to elevate his legs when seated. Two months postsurgery the flap repair has healed well and there is no evidence of metastatic disease (*Figure 6*).

## Summary of important points

- Always obtain histology to confirm a clinical diagnosis of keratoacanthoma (KA). Studies have shown that clinical KAs are just as likely to be SCCs. The converse is also true. Early histology is always required and will guide future management.
- Histology of a KA can also be difficult. Dermatopathologists frequently debate whether a lesion is KA or SCC. The histologic differences can be subtle. You may choose to have uncertain reports reviewed by an experienced dermatopathologist.
- The KA/SCC dilemma is best managed by treating all KAs as if they were well differentiated SCCs. Most authorities now regard a KA as a malignancy; although with slim metastatic potential.[2] These lesions can be removed by excision or curettage. This overcomes any clinical dilemma and eliminates the risk of a SCC developing a metastasis while it is 'watched'.
- SCCs at higher risk of developing metastases are recurrent tumours, those over 2 cm, and those on the ear, lip, eyelid or scalp. Transplant and immunosuppressed patients are also at increased risk of metastatic spread from their cutaneous SCC.
- One should not be avoiding excision because the defect would be too large to close. If the tumour needs excision, it needs excision. Delaying excision because defect closure is problematic is not acceptable. Consider referral either before or after biopsy as appropriate.

Figure 1. Tumour before debulking procedure

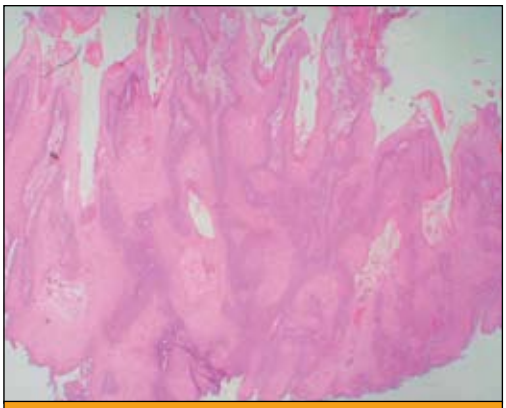

Figure 2. Papillary proliferation of mildly atypical squamous epithelium in this well differentiated invasive squamous cell carcinoma
Photo courtesy Melbourne Skin Pathology

Figure 3. Tumour 8 weeks before debulking procedure

Figure 4. Tumour 2 weeks before debulking procedure

## The challenge below the knee

Defects below the knee are a challenge for the clinician. All treatments have higher complication rates compared with other sites on the body. For example, we have demonstrated an infection rate below the knee of 7% compared with less than 1.5% above the knee.[3] All sites below the knee are subject to greater infection risk including the calf, shin, foot, and the toes. Even less 'invasive' measures such as cryotherapy and topical imiquimod can result in chronic ulceration in these sites.

We have demonstrated that the ROM flap reduces the risk of wound dehiscence, flap necrosis and overall complications when managing defects 11–45 mm below the knee.[4] We no longer use skin grafts unless the defect is greater than 45 mm in diameter.

Due to the increased infection risk below the knee, there is an argument for prophylactic antibiotics before surgery in these sites. We recommend 2 g oral dicloxacillin 1 hour before surgery. Above the knee, there are very few indications for antibiotic prophylaxis. Patients at high risk of endocarditis and patients with recent joint prosthetic surgery are special considerations.

Figure 5. Layout for excision and ROM flap repair

Figure 6. Wound healing 2 months postsurgery

Conflict of interest: none.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Melanoma with cutaneous melanoma secondaries

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case history**

Mr HG presented in 2002 with a large black lesion on his left loin. It had been present for many years but had recently changed (*Figure 1*). Nearby, two similar lesions were apparently separated by normal skin. Histology confirmed these were malignant melanoma. The 'normal' skin between lesions also demonstrated melanoma beneath the surface. At its thickest, this melanoma was a (Breslow) 2.56 mm, Clark 4 lesion. The tumour was excised with a minimum 20 mm margin of normal skin. Given the depth of the tumour, Mr HG was co-managed with the Victoria Melanoma Unit. There are no radiotherapy or chemotherapy programs that have been demonstrated to improve survival in patients with an advanced primary melanoma such as this. Following discussion, Mr HG chose not have a sentinel lymph node biopsy (SLNB).

**Mr HG had the opportunity to enroll in a randomised controlled trial (RCT) trial of emerging treatments. After discussion of his condition, prognosis and options, he and his wife declined to do so, instead choosing to buy a caravan and travel Australia.**

Mr HG remained well until he presented with a subcutaneous mass 10 cm from the primary site in 2004. On dissection, a black mass was excised (*Figure 2*). Histology confirmed this was metastatic melanoma (*Figure 3*). While scans in 2002 were clear, computerised tomography (CT) scans now showed pulmonary metastases. Despite the poor prognosis, the family continued to elect not to enter any emerging drug trial. The concern regarding 'numerous trips to Melbourne' was clear. The patient's wishes were respected.

In time, metastases developed elsewhere including numerous cutaneous and subcutaneous nodules (*Figure 4*). Most of the cutaneous nodules demonstrated the dermoscopic appearance of metastatic melanoma (*Figure 5*). Mr HG remained well through 2005. In this year he and his wife toured the USA and Europe. In early 2006 he became tired and nauseous. Anaemia was treated with transfusion. By this stage, subcutaneous and cutaneous masses were abundant. Cerebellar and cerebral secondaries affected gait and motor function. The inevitable decline continued. Mr HR succumbed to his melanoma in May 2006.

## Summary of important points

- While the majority of patients with melanoma present early and do well, the case study reminds us that melanoma is a potentially fatal condition.
- Melanoma management is not about fancy treatments in tertiary institutions. Effective management of melanoma is simply about early detection and wide excision. Nothing else improves long term outcome.[1,2]
- Subcutaneous metastases from any tumour are ominous with a 7.5 month average survival.[3] Lung cancer is the commonest cause of cutaneous secondaries (29%), melanoma is second (18%).
- Tests such as SLNB are not reasons to delay the treatment that matters – wide local excision. Even if the patient decides to undertake SLNB, this can be performed after the wide excision with no demonstrated difference in the accuracy of the test.[4]
- Patients with advanced melanoma should be offered the opportunity to enroll in trials of emerging treatments. We will not find that important breakthrough in future melanoma care without present day melanoma patients' participation in RCTs.
- Most commonly, metastatic deposits of melanoma have friable black contents, the histology merely confirms the clinically obvious.

Figure 1. Mr HG's primary malignancy with 'satellite' lesions

Conflict of interest: none.

Figure 2. Dissection of black subcutaneous mass 10 cm from original melanoma

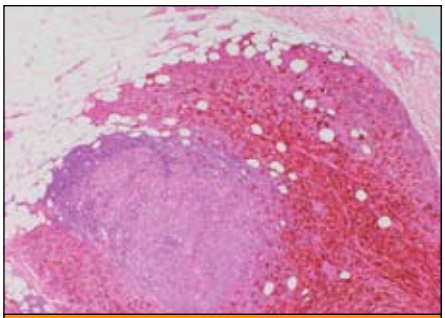

Figure 3. Histology of subcutaneous mass. Within subcutaneous fat is a deposit of metastatic melanoma. There are atypical epitheloid cells with adjacent macrophages containing melanin pigment

Photo courtesy Melbourne Skin Pathology

Figure 4. Mr HG's chest wall shows numerous cutaneous and subcutaneous deposits of metastatic melanoma

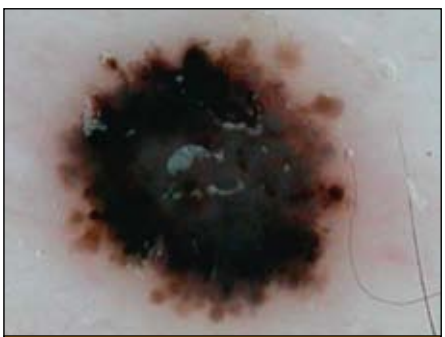

Figure 5. Dermoscopy of cutaneous metastaic melanoma. It has the appearance of malignant melanoma being 'sprayed' on to the site

## Sentinel lymph node biopsy

Sentinel lymph node biopsy (SLNB) has been popular in recent years, especially with patients suffering a melanoma beyond 1 mm thickness. The idea is to detect early evidence of melanoma in the lymph node that drains the skin at the site of the primary tumour. When nodes were found to contain melanoma, the patient usually progressed to having the entire nodal basin excised.[5]

However, there was always concern that such an intervention may not benefit the patient. We have known for some time through multiple RCTs that elective lymph node dissection on melanoma patients offers no survival benefit.[6]

10% of patients who undergo SLNB develop side effects and up to one-third of patients who go on to block dissection experience complications.[7] Complications include infection, seroma and lymphoedaema. More serious complications include facial nerve[8] and brachial plexus damage.[9]

Recently the first and only RCT of SLNB has demonstrated no survival benefit. Australia contributed many patients to this multi-national study known as MSLT-I. Concern has been expressed that the much presented trial has not yet been published.[10]

Further, many investigators have demonstrated that a sentinel node with only small amounts of melanoma in it may not subject the patient to added risk and the patient may not benefit from then proceeding to block dissection.[11–14]

As such, SLNB does not improve patient survival and does not guide further management. It does however, provide some added information to the patient regarding survival prospects as SLNB negative patients survive longer than positive patients.[15–17]

In 2006, SLNB is not a standard of care in melanoma management. It is an option for patients who wish to have further information about their prospects and are aware of the risks and complications of such an invasive procedure. Counselling before SLNB should include advice that the test does not guide future management.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Micronodular basal cell carcinomas

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mr AB developed a firm rough surface on his medial left cheek. With increasing size his doctor organised a biopsy at the site. Histology showed micronodular basal cell carcinoma (BCC). Tumour was excised with a margin of apparently normal skin. Histology showed tumour at all margins.

Some time later the borders of the skin wound revealed small nodules of obvious recurrence. Further surgery demonstrated tumour at all margins, once again. The wound was clinically clear and the area was managed expectantly. Later recurrence at margins was again apparent.

**Following an unsuccessful attempt with topical imiquimod, Mr AB was referred for margin control (slow Mohs) surgery. Mr AB had a large area on his medial left cheek with small nodules resembling a field of smooth bumps (*Figure 1*). He needed excision with no attempt to close the defect until histologic confirmation of clear margins. After two stages of slow Mohs surgery, the defect on his left cheek was significant (*Figure 2*). This defect was closed with a large trilobed flap repair with a burrows graft (*Figure 3*).**

Histology identified nodular and micronodular BCC in the dermis associated with a light chronic inflammatory infiltrate (*Figure 4*). Fortunately, Mr AB did not suffer any tumour invasion of the infraorbital nerve or its branches.

One year later there is no evidence of recurrence. The wound has healed reasonably other than a thickened scar near the border between nose and cheek (*Figure 5*). Mr AB elected not to have a small scar revision at this stage.

Figure 1. Note small, smooth bubbles appearing on cheek and an old linear scar

Figure 2. A large defect remains following histologic confirmation that tumour is cleared

## Summary of important points

- Micronodular basal cell carcinomas (BCCs) can look very innocuous. They are often large before they are diagnosed and margins are invariably very difficult to determine. Like morphoeic BCCs, they should be regarded as 'tough' and treated with respect.[1,2]
- Mohs surgery is the benchmark approach for micronodular BCCs on the face.[1,3,4]
- Imiquimod may be incorrectly considered for micronodular BCCs because they look thin and flat. Imiquimod is contraindicated for micronodular BCCs and is only indicated for superficial BCCs.[5–9]

- Proven residual BCC following surgery is not managed by observation. Some quarters hold to a misguided belief that the inflammatory process following surgery will 'kill off' any residual tumour. While the scar is 'watched', BCCs on the face can invade into many structures including nerves.

Figure 3. A trilobed flap did not close all the defect. A burrows graft completed the closure to the superomedial aspect of the defect

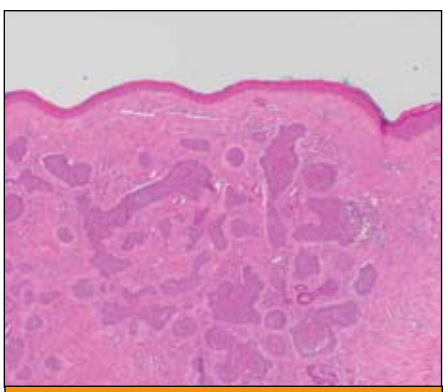

Figure 4. Micronodular and nodular BCC within the dermis
Photo courtesy Melbourne Skin Pathology

Figure 5. 12 months postsurgery

### The face is different

From a skin cancer perspective, the face is different in many respects.

Tumours look different: skin on the face is more pilo-sebaceous than elsewhere; the lower nose is especially pilo-sebaceous. This makes tumours often appear more subtle than they actually are. Dermoscopy of face lesions is altered by this pilo-sebaceous character. Pigment networking is often not seen and tumour features are less striking.

Structures are close: nerves, muscle, bone, cartilage, salivary glands and other structures can be very close to the skin surface and can be vulnerable at excision. Proximity also means tumours can invade vital structures if they extend beyond the dermis.

Caution with less invasive treatments: imiquimod and photodynamic therapy (PDT) on the face have special concerns. The therapy can fail while the tumour continues to invade into deeper structures. Sometimes imiquimod or PDT is chosen to 'avoid' surgery only to result in delayed much larger surgery.

Cosmetic features: the face has a myriad of cosmetic zones and features. These lines, borders and structures are always considerations in planning surgery and especially the repair of defects following surgery.[10–13]

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# High risk squamous cell carcinoma

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mrs MA, 70 years of age, has a history of scalp psoriasis dating over 10 years. She explained that the rash was slowly progressing and had failed to respond to an array of topical treatments offered (*Figure 1*).

Within the right lateral aspect of the 12 x 14 cm lesion a thick nodule had recently developed. It looked like squamous cell carcinoma (SCC). Biopsy of the raised lesion confirmed SCC as did four other biopsies at the poles of the region of 'psoriasis'. Removing all surface debris confirmed this was one confluent scalp tumour (*Figure 2*).

The large scalp SCC was excised with a 5 mm margin. During surgery there was an area of apparent involvement of galea. This layer was widely excised along with periosteum at that point. Histology confirmed complete excision. There was no other point at which deep levels were involved. Periosteum was not involved.

The large defect was closed with a partial thickness skin graft (*Figure 3*) harvested from the right anterior thigh (*Figure 4*).

**Mrs MA was assessed by the multidisciplinary head and neck team. Computerised tomography (CT) scans revealed cervical nodes that were not considered significant. She was considered for radiotherapy given the increased risk of metastasis associated with such a large long standing SCC. She was not keen on any further intervention and this wish was respected.**

Twelve months postsurgery there was no sign of local or regional recurrence. Mrs MA will have a permanent unsightly graft of skin covering most of the top of her scalp (*Figure 5*). She routinely wears a hat to cover the thin bald patch. (However, as she was wearing a hat for over 10 years to cover her psoriasis, this does not worry her and she is now quite accustomed to it.)

## Summary of important points

- If a skin condition does not respond to management as expected, biopsy the region rather than continue with the unsuccessful treatment. An unexpected malignancy may be identified.
- Partial thickness skin grafts are generally reserved for the largest of defects where other closures can be problematic. These grafts are invariably unsightly and lack the character of normal skin.

Figure 1. Scalp of presentation showing debris and matting of hair

Figure 2. Scalp with surface material removed showing large SCC

Figure 3. Scalp following wide excision of SCC and application of partial thickness skin graft

Figure 4. Partial thickness skin graft donor site on anterior right thigh

### High risk SCCs

Some cutaneous SCCs are recognised as at increased risk of developing metastatic disease. Most metastases occur within 2 years and 95% have occurred within 5 years. Surgery and adjuvant radiotherapy provide the best chance of achieving locoregional control.[1] Risk factors for metastases from cutaneous SCC are:

- recurrence[2–4]
- large tumours (>2 cm)[2,3]
- perineural involvement[2,3]
- poorly differentiated tumours[2,3]
- tumours infiltrating well into or beyond the dermis[3,5,6]
- renal (and other) transplant patients[7,8]
- immunosuppressed patients[3,8]
- tumours located on ear[3,9,10,] lip,[3,9–11,] eyelid[12] or sites that get no light.[3,13]

Figure 5. Thin bald graft 12 months postsurgery

- Radiotherapy is problematic in this situation, as split grafts do not tolerate radiation as well as full thickness skin. Chronic poor healing can result.
- Patients with large tumours on the head can benefit from the collective experience and opinions of skin surgeons, radiation oncologists, ENT surgeons and medical oncologists.

Conflict of interest: none declared.

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afp **CORRESPONDENCE** email: afp@racgp.org.au

# Arc welding and the risk of cancer

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mrs LF, 71 years of age, presents with numerous squamous cell carcinomas (SCCs) on her hands (*Figure 1*). She comments that she had 'perfect' hands until recent years and had never been an 'outdoors person'. On questioning her about trauma or exposure to her hands she commented that she had frequently experienced 'sunburn' on her hands after assisting her son with his welding business.

It turns out her son had started his own handyman business 10 years earlier. Most of the work involved arc welding repair jobs on fences and gates. He had bought a 240 volt welding unit and set up a mobile welding service out of his utility van. He had no money for staff, yet often needed an assistant to hold metal pieces to be welded together. Mum came to his rescue! She describes holding the metal with her bare hands and looking away to either the left or right while her son welded the sections. Her son wore a face mask, but sometimes did not wear gloves due to the hot conditions. This unfavourable health and safety story was supported by examination of Mrs LF's skin. She had marked actinic damage on her hands and forearms, but none on her chest (*Figure 2*), abdomen, back or lower limbs. Her face demonstrated actinic damage and two SCCs. Her neck also demonstrated marked actinic damage with a basal cell carcinoma on the right side (*Figure 3*) and a SCC on the left (*Figure 4*).

**Arc welding produces substantial ultraviolet (UV) radiation including the A (400–315 nm), B (315–280 nm) and C (280–100 nm) spectrums. Little is known of the damage that can be caused by UVC because humans are rarely exposed to such short wavelength UV radiation.[1–3] Virtually all solar UVC is absorbed in the atmosphere long before it reaches the earth's surface.[3,4] In contrast, UVC from arc welding is mostly absorbed by air immediately around the arc, but some could reach exposed skin on the welding operator.**

The cause and effect relationship between arc welding and skin cancer has not been demonstrated to date, however there has been little research into this occupational hazard. One study showed no increased incidence of skin cancer in welders.[5] However, this study involved a plant with very high health and safety standards and workers were well protected with mask and clothing whenever welding. Greater concern surrounds workplaces where health and safety standards may be suboptimal, such as farmers, sculptors, tradesmen and mechanics who may undertake welding without formal training.[4]

Different welding processes produce variation in the degree of UV exposure for the worker and any assistant. UV exposure is increased with: decreasing proximity to

Figure 1. Numerous SCCs have developed on both hands and forearms on a background of marked actinic damage

Figure 2. The chest, back and lower limbs are without actinic change

Figure 3. The right neck shows a morphoeic BCC

Figure 4. The left neck shows a well differentiated SCC. The face is markedly damaged with smaller SCCs needing attention

**Table 1. Welding process and the degree of UV radiation produced**

| UV level | Welding process | Distance in metres for 1 minute duration before US daily threshold limit of UV is reached while welding mild steel |
|---|---|---|
| High | Gas metal arc welding | 0.95 m at 90 amps |
| | Gas tungsten arc welding | 0.90 m at 150 amps |
| Medium | Most shielded metal arc welding including domestic units | 3.2 m at 100 amps |
| Low | Submerged arc welding | Beyond any distance of concern |
| Minimal or nil | Oxy-acetylene welding | Minimal UV |
| | Resistance welding | |
| | Friction welding | |
| | Friction stir welding | |

Source: Lyon TL. Evaluation of the potential hazards for actinic ultraviolet radiation generated by electric welding and cutting arcs. US Army Environmental Hygiene Agency, 1976

the arc, increased arc energy, increased arc duration, higher current and certain angles of plate reflection. Different welding processes produce different UV exposure (*Table 1*).[6] The most intense UV exposure is often associated with welding aluminium or stainless steel where gas metal arc (GMA) or gas tungsten arc (GTA) processes are often used. It is an imperative that arc welders and their assistants wear suitable gloves, forearm clothing, mask, and protection for the neck (*Figure 5, 6*).

Figure 5. An example of unsafe welding practice. Note the bare hands and forearms. The welder is working close to the arc and his neck is also unsafely exposed

Figure 6. A safer GTA welding practice. This welder should also have protection to the back of the neck as well some fume extraction system in place.
Reproduced with permission: Prototype Engineering Centre, 2006

Skin is not the only organ at risk from arc welding.[7] Fumes from the welding process are linked with pulmonary disease and other diseases.[8,9] Eye damage from arc welding is also well established.[10–13]

## Summary of important points

- Arc welding may be a contributory cause of skin cancer in some patients, especially when a history of lack of protection is apparent.
- Welders and their assistants need advice regarding suitable protection when arc welding (*Figure 6*).
- Anyone can buy an inexpensive arc welding unit from the hardware store without any training in its use. Part time welders such as farmers and tradesmen may be unaware of the risks.
- Welders should use sunblock for the protection of exposed skin. Some sunscreens specifically include UVC protection and welders can be encouraged to select these products.
- Arc welding aluminium produces the most intense UV radiation due to high arc energies involved and high reflectivity of the metal surface.
- Other occupational causes of skin cancer are usually associated with solar ultraviolet. These include outdoor workers such as road workers, gardeners and farmers.

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Rare skin cancers in general practice

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mr LA has long been troubled with actinic damage to his skin, especially his face. He has had many squamous cell carcinomas (SCCs) removed and many solar keratoses managed.

On this occasion Mr LA had two actinic lesions on his left cheek that failed to respond to cryotherapy (*Figure 1*). A biopsy of each site produced a surprise. Histology of the superior lesion revealed sebaceous carcinoma (*Figure 2*). This is an uncommon yet aggressive cutaneous malignancy derived from sebaceous glands. The 5 year survival rate is 60–70%.

The tumour was widely excised with a minimum 10 mm margin. A multidisciplinary approach resulted in a decision not to proceed to adjunctive radiotherapy. The wound was well healed by 8 weeks (*Figure 3*). Four years on there is no sign of local or regional recurrence (*Figure 4*).

**Many sebaceous carcinomas occur on the eyelids where the outcome is often poor;[1] and some patients are prone to multiple other cutaneous SCCs.**

There is also a rare syndrome called Muir-torre of visceral neoplasms associated with sebaceous carcinoma on the skin.[2] As this is an autosomal dominant condition, family history and counselling is an esssential part of management (enquire about family history of internal malignancies). A family member's diagnosis can be important for other family members and offers screening for internal and cutaneous malignancies.

Mr LA's tumour reminds us that among the basal cell carcinomas (BCCs), SCCs and melanomas removed in large numbers in Australia every day, there are unusual malignancies that we may come across from time-to-time. While we have large studies comparing management options in the more common cutaneous malignancies, it is rarely possible to have large management trials of tumours that none of us see frequently. Treatment is less clear and needs several good minds working together.

The relative severity of some of the rare tumours is tiered and summarised in *Table 1*. Sarcomas generally have among the poorest outcomes.[3]

Figure 1. Two actinic lesions on the left face have failed to respond to cryotherapy

Figure 3. Satisfactory healing 8 weeks following wide excision of sebaceous carcinoma

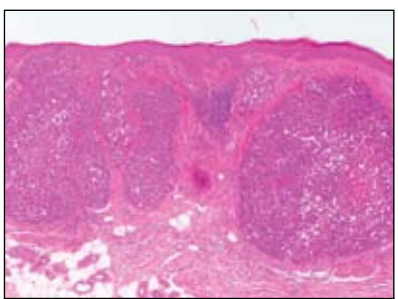

Figure 2. Within the dermis are lobules of epithelial cells showing cytoplasmic vacuolation, mitoses, and nuclear atypia characteristic of sebaceous carcinoma
Photo courtesy Melbourne Skin Pathology

Figure 4. Four years postsurgery there is no regional recurrence

## Summary of important points

- Rare tumours don't get diagnosed clinically. They are invariably diagnosed as a 'surprise' on the histology report.[3]
- Consider biopsy of the atypical or recalcitrant actinic keratoses before proceeding to another 'freeze'.
- Send every specimen to the histologist, not the bin. A clinical sebaceous cyst, wart, seborrhoeic keratosis

**Table 1. Some rare skin malignancies and management considerations (tumours are ordered from the most to least fatal)**

| Tumour | 5 year survival | Clinical characteristics | Surgery involved | Chemotherapy involved | Radiation involved |
|---|---|---|---|---|---|
| Cutaneous angiosarcoma (AS)[5,6] | 15% | Mostly on face, scalp, or breast. Local recurrence and metastatic spread frequent, especially to lung. Can occur in postradiation scar | Very wide local excision | Often | Often |
| Merkel cell carcinoma (MCC)[7–9] | 40–68% | Local recurrence common even after very wide surgery. Mostly on head and neck. Spontaneous regression can occur | Mohs or very wide surgery | Occasionally | Often |
| Sebaceous carcinoma (SC)[1,2,10] | 60–70% | Often subcutaneous, often on eyelids or scalp. Can be associated with visceral tumours | Verywidelocal excision | No | Often |
| Dermatofibrosarcoma protuberans (DFSP)[9,11–13] | 93+% | Local recurrence/destruction in 50–75% of cases; can be fatal. <5% metastasise. Can look like a morphoeic BCC. Often extends well beyond apparent borders. Typically in young/ middle aged with predilection for pectoral and pelvic regions | Mohs surgery ideal | Limited | Some |
| Digital papillary adenocarcinoma[14] | 95% | Occurs on the digits. Often looks encapsulated and hence less aggressive than the reality. Metastasises frequently to lungs | Amputate digit | Some | Often |
| Microcystic adnexal carcinoma (MAC)[5,9] | 99% | Behaves like aggressive BCC. High local recurrence risk. 90% are on head and neck | Mohs surgery ideal | Some | Some |
| Eccrine adenocarcinoma[15,16] | 99+% | Behaves like aggressive BCC. Many around eye. Many subtypes. High local recurrence risk | 4 mm margin excision | No | No |
| Atypical fibroxanthoma (AFX)[17–19] | 99+% | Low grade sarcoma. Behaves like a BCC. Metastasis very rare. Most occur on elderly, sun damaged head and neck skin. Can occur in old radiation scars | 4 mm margin excision | No | No |
| Kaposi sarcoma (KS)[20,21] | Death from other cause | Three subtypes:<br>• elderly of Jewish/Mediterranean descent<br>• immunosuppressed (eg. postrenal transplant)<br>• HIV/AIDS related | No | Often | Usual |

or lipoma can sometimes lead to such a 'surprise'.[4]

- Consult with colleagues and consider involving multidisciplinary experts in management of that surprise unusual tumour. Management predominantly involves surgery but can involve adjunctive radiotherapy or chemotherapy (*Table 1*).
- Unusual tumours are often diagnosed late and many have poor prognoses.
- Sometimes a small biopsy may not provide the answer and complete local excision is required for histologic diagnosis.[3]
- Check whether there are management trials for possible enrolment of your patient with an unusual tumour.

Conflict of interest: none.

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afp **CORRESPONDENCE** email: afp@racgp.org.au

# Managing bleeding complications in skin surgery

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mr AB, aged 78 years, developed a lentigo maligna (LM) on his left cheek just below the orbital margin (*Figure 1*). Dermoscopy was typical for LM, with thickened variable peri-follicular pigmentation, some granular pigmentation, and an area of regressive depigmentation (*Figure 2*). Mr AB has a past history of aortic valve replacement and has been taking warfarin prophylaxis for many years.

The tumour was excised with a 6 mm margin and effected a laterally based transposition flap. Warfarin was not ceased either before or after surgery. A small bleed occurred from the wound 2 days postsurgery. Redressing was effected but no other intervention was required. Sutures were removed on day 8. Two days after removal of sutures, Mr AB bumped his left cheek in a stumble and the wound started bleeding again. He developed a haemorrhage under the flap resulting in significant haematoma (*Figure 3*), flap necrosis, and subsequent ulceration (*Figure 4*) at the site. This required wound toileting and repeated dressings in a prolonged postoperative course. Over time, the wound healed with conservative management (*Figure 5*).

## Bleeding complications in skin surgery

The following points about bleeding complications are relevant to Mr AB's case:

- Postoperative bleeds from abdominal, brain and chest surgery can be catastrophic, but no life threatening bleed has ever been reported following cutaneous surgery[1,2]
- Surgeons often claim to be able to tell during surgery whether or not the patient is on anticoagulants. The evidence suggests surgeons cannot make such a differentiation[3]
- In skin surgery, most complications are managed by conservative measures such as toileting the wound, applying pressure and applying dressings. Antibiotics are sometimes required for overt wound infection
- Operative intervention for skin surgery complications is rare. If a bleed is active and ongoing then surgical control of the bleeding may be required. If the bleed is old and stable, nature and time will invariably sort the matter out
- Diathermy, preferably bipolar, should be available for skin surgery cases so as to control and minimise any intra-operative bleeding when this does happen.

At our Geelong (Victoria) based skin cancer centre we completed a prospective study from July 2002 until October 2006 of 6000 patients looking at the effects of thrombosis preventive medication on skin surgery.[4] Patients did not have their aspirin or warfarin ceased unless the International Normalised Ratio (INR) was greater than three. In 6000 cases, the postoperative bleeding incidence was 0.67%.[4] There were four independent risk factors for postoperative bleeding:

- warfarin management
- surgery in or near the ear
- age over 67 years, and
- closure with flap or graft.

*Table 1* demonstrates how the risk of bleeding increases as these four risk factors accumulate. The study found that aspirin is not an independent risk factor for postoperative

**Table 1. The risk of bleeding complications for patients grouped by the number of bleeding risk factors in 6000 consecutive cases[4]**

| Number of risk factors | Overall bleeding rate |
|---|---|
| 0 | 1 in 1000 |
| 1 | 4 in 1000 |
| 2 | 12 in 1000 |
| 3 | 43 in 1000 |
| 4 | 56 in 1000 |

bleeding. There is no case for ceasing aspirin for skin surgery.

Warfarin may be ceased if the risks of continuation outweigh the benefits. This is only likely when three or more of the identified risk factors are present. However, warfarin should never be ceased within 1 month of a life threatening thromboembolic event.[5] Warfarin should invariably be continued in patients undergoing leg surgery given that reduced mobility following such surgery compounds the thromboembolic risk to the patient. If continuing warfarin, ensure the INR level before and after surgery is in the therapeutic range.[6]

Newer agents such as clopidogril and ticlopidine were not included in this prospective study as they were not in common usage during the design phase of the study. No advice can be drawn on the ceasing or otherwise of these newer agents. The study found that smoking and diabetes were not risk factors for postoperative bleeding.

Discussion of the role of short term subcutaneous heparins is now somewhat moot and supports previous studies[2] demonstrating that there is little if any case for a switch to short term heparins to effect skin surgery. The main consideration in the past has been for leg excisions requiring prolonged immobilisation. Immobilisation is not commonly required with more current approaches below the knee.[7] It would now only be considered with skin graft surgery for large defects >5 cm diameter.[6] Defects of this size account for around 1% of skin defects arising from elective excision of skin lesions below the knee.

When managing melanoma, given a 1 cm margin of normal skin is usually appropriate,[8–10] a melanoma would need to be around 3 cm in diameter to result in a 5+ cm defect.

Figure 1. LM on left cheek. Surgery in this region must ensure there is no pull that might result in ectropion

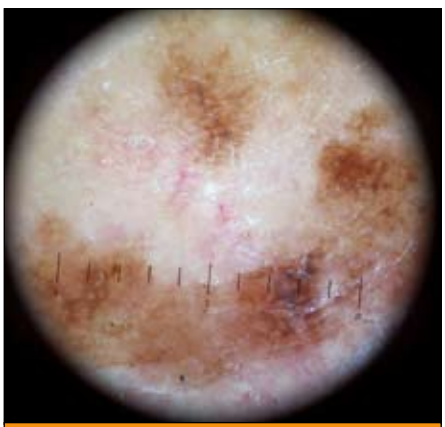

Figure 2. Dermoscopy of the LM

Figure 3. A large haematoma develops

Figure 4. As the bleed matures an area of ulceration develops

Figure 5. Despite the graphic appearance following the bleed, the wound settles

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au

# Treating actinic keratoses with imiquimod

**Anthony Dixon**
MBBS, FACRRM, is dermasurgeon and Director of Research, Skin Alert Skin Cancer Clinics and Skincanceronly, Belmont, Victoria. anthony@skincanceronly.com

**Case study**

Mr KC, 61 years of age, has extensive actinic damage including squamous cell carcinomas (SCCs) and actinic keratoses (AKs) on his face and forehead. He has had cryotherapy for many years with limited success. Lesions have generally resolved with cryotherapy but he finds the treatment very uncomfortable and can only tolerate a small number of lesions being treated on each visit. He develops lesions faster than lesions are treated.

**Mr KC now presents with numerous hyperkeratotic lesions on his face (*Figure 1*). Biopsies were taken of the clinically most suspicious actinic lesions. This is done to identify which, if any, lesions are SCCs. (These are surgically excised.) Numerous actinic keratoses still covered most of his face including most of his left forehead.**

He was keen to try imiquimod for his residual actinic keratoses. We divided his face up into regions about the size of a playing card. In turn he treated each region with an application of imiquimod three times per week for 6 weeks. This is the recommended protocol for usage of imiquimod for actinic keratoses.

The final section of face skin to be treated was the right forehead. Mid treatment the area was red and angry looking, as part of the expected immune response induced by the imiquimod[1] (*Figure 2*). This erythema and irritation was never disturbing to the patient. If imiquimod causes excess irritation, the clinician can advise the patient to leave out a dose or two. Upon completion Mr KC had no apparent actinic lesions on his face or forehead (*Figure 3*).

## Summary of important points

- Treat malignant lesions before benign lesions. It is the SCCs that can metastasise and potentially kill patients. Once the SCCs are excised, the focus can turn to the premalignant lesions.
- There are many options for managing actinic keratoses. Percentage complete clearance of lesions with cryotherapy is in the order of 80%, topical imiquimod 70% and 5 fluorouracil 50%.[2–5]
- Some patients will find some of the options more tolerable than others. Consider trying alternative approaches for patients with

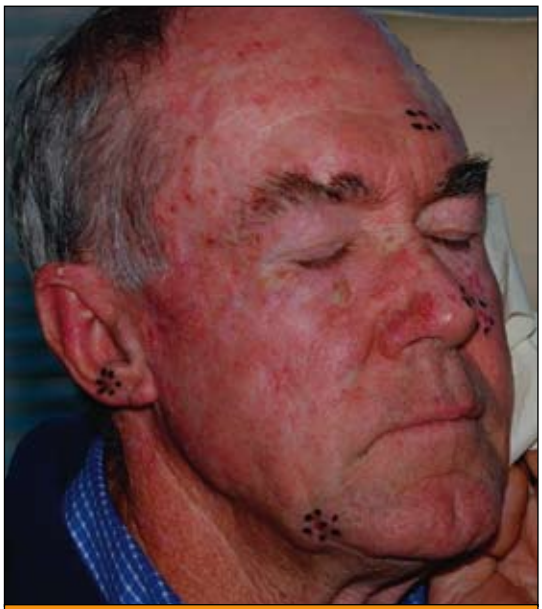

Figure 1. The patient's face is covered with actinic lesions, especially the forehead. The lesions marked with pen are all SCCs and were surgically excised. There was further SCC on the right eyebrow, also surgically excised

Figure 2. The skin is typically red and angry looking for the duration of imiquimod management of actinic keratoses. Imiquimod was only commenced following all surgical excisions

### Numerous actinic keratoses

There are five characters of an actinic keratosis that should be considered upon examination:

- **Hyperkeratosis:** to what extent does the keratosis extend above the skin surface?
- **Full thickness:** when the lesion is manipulated with your fingers upon examination, does it appear to be deeply into the skin or very much a surface structure?
- **Surrounding induration:** is there enhanced thickness in the tissue adjacent to the keratosis?
- **Surrounding erythema:** is the immediate adjacent skin clearly redder than the background skin colour?
- **Tenderness:** is the lesion causing the patient any degree of discomfort? Does the patient withdraw when you touch one or more lesions in the field of lesions you examine?

The more of these characteristics an individual lesion has, the more likely the lesion is to be a malignant SCC rather than a premalignant lesion. In patients with large numbers of keratoses, consider biopsy of the lesions that have the greatest number of these features.

Regardless of the number of keratoses a patient suffers, lesions with three or more of these five features should be biopsied.

If any lesion demonstrating several of these features does not respond to cryotherapy, biopsy rather than treating repeatedly with cryotherapy or imiquimod or 5 fluorouracil.

Figure 3. Following treatment there is no apparent residual actinic lesions

numerous AKs. Allow the patient to discover with you which management option works best for them.

- Imiquimod is approved in Australia for field actinic keratoses only on the face and forehead. The patient applies a full sachet three times per week to an area of skin equivalent to the forehead on one side. One sachet will cover a field about this size. Once one region has completed management, a new region may be commenced.

Conflict of interest: none declared.

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afp CORRESPONDENCE email: afp@racgp.org.au